09/007,093

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********** STN Columbus **********

FILE 'HOME' ENTERED AT 15:26:51 ON 30 MAR 1999

=> file medline cancerlit biosis scisearch embase wpids

FILE 'MEDLINE' ENTERED AT 15:27:13 ON 30 MAR 1999

FILE 'CANCERLIT' ENTERED AT 15:27:13 ON 30 MAR 1999

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FILE 'WPIDS' ENTERED AT 15:27:13 ON 30 MAR 1999
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[redacted]s (antibod? or monoclon?) and (apc or dendritic cell or macrophage or
langerhans cell or kupffer cell or antigen presetning cell)

  1 FILES SEARCHED...
  2 FILES SEARCHED...
  5 FILES SEARCHED...
L1      55397 (ANTIBOD? OR MONOCLON?) AND (APC OR DENDRITIC CELL
OR MACROPHAGE
        OR LANGERHANS CELL OR KUPFFER CELL OR ANTIGEN
PRESETNING CELL)

=> s l1 and (conjugate or chimer? or fusion(w)protein)

L2      1370 L1 AND (CONJUGATE OR CHIMER? OR FUSION(W) PROTEIN)

=> s l2 and adjuvant

L3      58 L2 AND ADJUVANT

=> dup rem

ENTER L# LIST OR (END):l3

PROCESSING COMPLETED FOR L3
L4      34 DUP REM L3 (24 DUPLICATES REMOVED)

=> d l4 1-34 ibib ab

[redacted]  ANSWER 1 OF 34  SCISEARCH  COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER:   1999:91619  SCISEARCH
THE GENUINE ARTICLE: 158UJ
TITLE:          A human immunodeficiency virus type 1 Env-granulocyte-
                macrophage colony-stimulating factor
                fusion protein enhances the cellular
                immune response to Env in a vaccinia virus-based vaccine
AUTHOR:         Rodriguez D; Rodriguez J R; Llorente M; Vazquez I; Lucas
                P; Esteban M (Reprint); MartinezA C; delReal G
CORPORATE SOURCE:   UNIV AUTONOMA MADRID, CSIC, CTR NACL
BIOTECNOL, DEPT MOL &
                CELLULAR BIOL, CAMPUS CANTOBLANCO, E-28049 MADRID,
SPAIN
                (Reprint); UNIV AUTONOMA MADRID, CSIC, CTR NACL
BIOTECNOL,
                DEPT MOL & CELLULAR BIOL, E-28049 MADRID, SPAIN; UNIV
                AUTONOMA MADRID, CSIC, CTR NACL BIOTECNOL, DEPT
IMMUNOL &
                ONCOL, E-28049 MADRID, SPAIN
COUNTRY OF AUTHOR:   SPAIN
SOURCE:         JOURNAL OF GENERAL VIROLOGY, (JAN 1999) Vol. 80,
Part 1,
                pp. 217-223.
                Publisher: SOC GENERAL MICROBIOLOGY, MARLBOROUGH
HOUSE,
                BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AE,
BERKS,
                ENGLAND.
                ISSN: 0022-1317.
DOCUMENT TYPE:      Article; Journal
FILE SEGMENT:       LIFE
LANGUAGE:           English
REFERENCE COUNT:    29
                *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB      Vaccinia virus (VV) infection induces protective T- and B-cell
        responses, making recombinants based on VV good candidates for the
        development of effective vaccines to other viruses, VV recombinants
        expressing the human immunodeficiency virus (HIV) envelope protein (Env)
        have been generated in several laboratories and shown to induce anti-HIV
        cellular and humoral immune responses in vaccinated humans and in
        chimpanzees. To increase the immunogenicity of the Env antigen, a VV
        recombinant was generated that expresses a chimeric antigen
        consisting of the Env protein fused to an immunostimulatory cytokine,
        granulocyte-macrophage colony-stimulating factor (GM-CSF), The
        chimeric protein retained GM-CSF biological activity when
        expressed by this recombinant virus (VV-GM-gp120) in cells infected in
        vitro, Infection of BALB/c mice with VV-GM-gp120 triggered a higher
        HIV-specific cellular immune response, as measured by interferon-gamma
        production, than that induced by a VV recombinant expressing the native
        Env protein. Moreover, although anti-gp120 antibody titres were
        similar in sera from mice inoculated with either of the VV recombinants,
        immunization with the recombinant expressing the fusion
        protein elicited antibodies against a broader spectrum
        of Env epitopes, These results indicate that HIV Env antigen fusion to
        GM-CSF provides a means to improve the anti-HIV immune response.

L4  ANSWER 2 OF 34  WPIDS  COPYRIGHT 1999 DERWENT INFORMATION
LTD
ACCESSION NUMBER:   99-023378 [02]  WPIDS
CROSS REFERENCE:    86-320618 [49];  88-316484 [45]
DOC. NO. CPI:       C99-007032
TITLE:          Inducing cytotoxic T cell response against virus using
                peptide-fatty acid conjugate - formulated in
                liposomes with an adjuvant, specifically for
                protecting against herpes simplex or rabies viruses.
DERWENT CLASS:      B04
INVENTOR(S):        DIETZSCHOLD, B; HEBER-KATZ, E
PATENT ASSIGNEE(S):  (WIST-N) WISTAR INST
COUNTRY COUNT:      1
PATENT INFORMATION:

  PATENT NO KIND DATE  WEEK   LA  PG
  -------------------------------------
  US 5837249  A  981117 (9902)*    21

APPLICATION DETAILS:

  PATENT NO  KIND          APPLICATION    DATE
  ----------------------------------------------
  US 5837249  A  CIP of       US 85-725087   850419
                 Cont of      US 87-47443    870508
                 CIP of       US 91-685459   910412
                 Cont of      US 92-868946   920415
                              US 93-139609   931020


PRIORITY APPLN. INFO: US 92-868946  920415; US 85-725087  850419; US
                87-47443  870508; US 91-685459  910412; US
                93-139609  931020
AB  US 5837249 A  UPAB: 990113
    A cytotoxic T cell response is induced in a mammal against viral infection
    by administering a peptide-fatty acid conjugate of formula (I),
    formulated with a liposome and adjuvant, such that the peptide
    component protrudes from the liposome.
      R'-CONH-(CH2)4-CH(NHCOR")-CONH-spacer-peptide-COOR'"  (I)
      R' and R" = 5-30C alkyl;
      R'" = H or at least one amino acid residue;
      the peptide has the sequence of a fragment of viral protein that can
    produce a protective T cell response.
      Also claimed is a vaccine against herpes simplex virus (HSV) types I
    or II comprising specific (I), liposomes and an adjuvant.
      USE - (I) are used particularly to vaccinate against HSV, rabies and
    also other viruses such as influenza, human immune deficiency virus and
    oncogenic viruses.
      (I) is administered to provide 0.1-0.3(especially 0.15) mg peptide
    per dose.
      ADVANTAGE - When the liposomes fuse to an antigen-presenting cell (
    APC), (I) remains bound to the surface of the APC
    membrane and is not degraded inside the cell, which generates a T cell
    response without any antibody response, avoiding the risk of
    immune enhancement (in which antibodies increase viral
    infectivity).
      (I) can provide long-lasting protection from only a single injection.
    Dwg.1/7

L4  ANSWER 3 OF 34  EMBASE  COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   1998390444  EMBASE
TITLE:          Immunostimulatory CpG oligodeoxynucleotides enhance the
                immune response to vaccine strategies involving
                granulocyte-macrophage colony-stimulating factor.
AUTHOR:         Liu H.-M.; Newbrough S.E.; Bhatia S.K.; Dahle C.E.; Krieg
                A.M.; Weiner G.J.
CORPORATE SOURCE:   Dr. G.J. Weiner, Department of Internal Medicine,
                University of Iowa, 200 Hawkins Dr, Iowa City, IA 52242,
                United States
SOURCE:         Blood, (15 Nov 1998) 92/10 (3730-3736).
                Refs: 38
                ISSN: 0006-4971  CODEN: BLOOAW
COUNTRY:        United States
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       016  Cancer
                    025  Hematology
                    026  Immunology, Serology and Transplantation
                    037  Drug Literature Index
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB  Immunostimulatory oligodeoxynucleotides containing the CpG motif (CpG
ODN)
    can activate various immune cell subsets and induce production of a number
    of cytokines. Prior studies have demonstrated that both CpG ODN and
    granulocyte-macrophage colony-stimulating factor (GMCSF) can
    serve as potent vaccine adjuvants. We used the 38C13 murine lymphoma
    system to evaluate the immune response to a combination of these two
    adjuvants. Immunization using antigen, CpG ODN, and soluble GM-CSF
    enhanced production of antigen-specific antibody and shifted
    production towards the IgG2a isotype, suggesting an enhanced TH1
response.
    This effect was most pronounced after repeat immunizations with CpG ODN
    and antigen/GMCSF fusion protein. A single
    immunization with CpG ODN and antigen/GM-CSF fusion
    protein 3 days before tumor inoculation prevented tumor growth.
    CpG ODN enhanced the production of interleukin-12 by bone marrow-derived
    dendritic cells and increased expression of major histocompatibility
    complex class I and class II molecules, particularly when cells were
    pulsed with antigen/GM-CSF fusion protein. We conclude
    that the use of CpG ODN in combination with strategies involving GM-CSF
    enhances the immune response to antigen and shifts the response towards
a
    TH1 response and that this approach deserves further evaluation in tumor
    immunization approaches and other conditions in which an antigen-specific
    TH1 response is desirable.

L4  ANSWER 4 OF 34  EMBASE  COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   1998399381  EMBASE
TITLE:          Soluble proteins modified with acetaldehyde and
                malondialdehyde are immunogenic in the absence of
                adjuvant.
AUTHOR:         Thiele G.M.; Tuma D.J.; Willis M.S.; Miller J.A.; McDonald
                T.L.; Sorrell M.F.; Klassen L.W.
CORPORATE SOURCE:   Dr. G.M. Thiele, Omaha Veterans Admin. Medical
Center,
                Research Service 151, 4101 Woolworth Avenue, Omaha, NE
                68105, United States
```

09/007,093

SOURCE: Alcoholism: Clinical and Experimental Research, (1998) 22/8 (1731-1739).
Refs: 63
ISSN: 0145-6008 CODEN: ACRSDM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recent studies have shown that the alcohol metabolites malondialdehyde and acetaldehyde can combine to form a stable adduct (MAA) on proteins. This adduct has been detected in the livers of rats chronically consuming ethanol, and serum **antibodies** to MAA have been observed at significantly higher concentrations in ethanol-fed when compared with pair-fed or chow-fed control rats. More recently, preliminary studies have strongly suggested that the MAA adduct is capable of stimulating **antibody** responses to soluble proteins in the absence of adjuvants. The **antibodies** produced recognize either the MAA epitope or the carrier protein itself. Therefore, it was the purpose of this study to examine the potential immunogenicity of MAA-modified exogenous proteins in the absence of adjuvants. Balb/c mice were immunized in the presence or absence of **adjuvant** with different concentrations of unmodified or MAA-modified proteins. The **antibody** response to both the MAA epitope and unmodified protein epitopes were determined by ELISA. In the absence of **adjuvant**, significant **antibody** responses were induced to both the MAA epitope and nonmodified protein epitopes. Smaller immunizing doses of MAA-protein **conjugate** favored the production of **antibodies** to nonmodified proteins, whereas larger doses induced a strong anti-MAA response. In studies to begin determining a mechanism for the specificity of the response in the absence of adjuvants, peritoneal macrophages were found to bind and degrade MAA-adducted proteins through the use of a scavenger receptor. This indicated that MAA- adducted proteins may be specifically taken up and epitopes presented to the humoral immune system in the absence of adjuvants. Importantly, these are the first data showing that an alcohol-related metabolite can induce an **antibody** response in the absence of **adjuvant** and suggesting a mechanism by which **antibody** to the MAA adduct or its carrier (exogenous or endogenous) proteins may be generated in vivo.

L4 ANSWER 5 OF 34 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 1998:257629 SCISEARCH
THE GENUINE ARTICLE: ZD630
TITLE: Enhanced protective **antibody** responses to PspA after intranasal or subcutaneous injections of PspA genetically fused to granulocyte-**macrophage** colony-stimulating factor or interleukin-2
AUTHOR: Wortham C; Grinberg L; Kaslow D C; Briles D E; McDaniel L S; Lees A; Flora M; Snapper C M; Mond J J (Reprint)
CORPORATE SOURCE: UNIFORMED SERV UNIV HLTH SCI, DEPT MED, 4301 JONES BRIDGE RD, BETHESDA, MD 20814 (Reprint); UNIFORMED SERV UNIV HLTH SCI, DEPT MED, BETHESDA, MD 20814; UNIFORMED SERV UNIV HLTH SCI, DEPT PATHOL, BETHESDA, MD 20814; UNIFORMED SERV UNIV HLTH SCI, BIOMED INSTRUMENTAT CTR, BETHESDA, MD 20814; NIAID, PARASIT DIS LAB, NIH, BETHESDA, MD 20892; UNIV ALABAMA, DEPT MICROBIOL, BIRMINGHAM, AL 35294; UNIV MISSISSIPPI, MED CTR, DEPT SURG, JACKSON, MS 39216; UNIV MISSISSIPPI, MED CTR, DEPT MICROBIOL, JACKSON, MS 39216
COUNTRY OF AUTHOR: USA
SOURCE: INFECTION AND IMMUNITY, (APR 1998) Vol. 66, No. 4, pp. 1513-1520.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB **Antibody** to pneumococcal surface protein A (PspA) has been shown to be protective for Streptococcus pneumoniae infections in mice. In an attempt to define a model for inducing protective **antibody** to PspA in the absence of **adjuvant**, we designed two genetic fusions, PspA-interleukin-2 [IL-2]) and PspA-granulocyte-**macrophage** colony-stimulating factor (GM-CSF). These constructs maintained high cytokine function in vitro, as tested by their activity on IL-2 or GM-CSP-dependent cell lines. While intranasal immunization with PspA induced no detectable anti-PspA response, both PspA-IL-2 and PspA-GM-CSF stimulated high immunoglobulin G1 (IgG1) **antibody** responses, Interestingly, only the PspA-IL-2, not the PspA-GM-CSF, construct stimulated IgG2a **antibody** responses, suggesting that this construct directed the response along a TH1-dependent pathway. Comparable enhancement of the anti-PspA response with similar isotype profiles was observed after subcutaneous immunization as well. The enhancement observed with PspA-IL-2 was dependent on IL-2 activity in that it was not seen in IL-2 receptor knockout mice, while PspA in alum induced high-titer **antibody** in these mice, The **antibody** was tested for its protective activity in a mouse lethality model using S. pneumoniae WU-R2. Passive transfer of 1:90 dilutions of sera from mice immunized with PspA-IL-2 and PspA-GM-CSF elicited protection of CBA/N mice against intravenous challenge with over 170 50% lethal doses of capsular type 3 strain WU2, Only 0.17 mu g or less of IgG **antibody** to PspA was able to provide passive protection against otherwise fatal challenge with S. pneumoniae. The data demonstrate that designing protein-cytokine fusions may be a useful approach for mucosal immunization and can induce high-titer systemic protective **antibody** responses.

L4 ANSWER 6 OF 34 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 97-319786 [29] WPIDS
DOC. NO. CPI: C97-103321
TITLE: Stimulating release of **antibody** from B cells with granulocyte-**macrophage** colony stimulating factor - and/or interleukin-3, used to improve response to immunising antigens, also use of **antibodies** against these cytokine(s) in treatment of auto-immune disease.
DERWENT CLASS: B04 D16
INVENTOR(S): MOND, J J; SNAPPER, C M
PATENT ASSIGNEE(S): (JACK-N) JACKSON FOUND ADVANCEMENT MILITARY MED
COUNTRY COUNT: 21
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9720940 | A1 | 970612 (9729)* | | EN | 61 |
| RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE | | | | | |
| W: AU CA JP | | | | | |
| AU 9711465 | A | 970627 (9742) | | | |
| EP 866871 | A1 | 980930 (9843) | | EN | |
| R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9720940 | A1 | WO 96-US19327 | 961205 |
| AU 9711465 | A | AU 97-11465 | 961205 |
| EP 866871 | A1 | EP 96-942887 | 961205 |
| | | WO 96-US19327 | 961205 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 9711465 | A Based on | WO 9720940 |
| EP 866871 | A1 Based on | WO 9720940 |

PRIORITY APPLN. INFO: US 95-568343 951206
AB WO 9720940 A UPAB: 970716
Composition for stimulating release of **antibody** (Ab) from B cells comprises granulocyte-**macrophage** colony stimulating factor (GM-CSF) and/or interleukin-3 (IL-3).
Also claimed are:
(1) **conjugate** vaccine (CV) containing:
(i) GM-CSF and/or IL-3 and
(ii) vaccinating antigen (Ag), both components bound to a multivalent carrier, and
(2) neutralising vaccine **adjuvant** (NVA) comprising at least 1 **antibody** directed against GM-CSF, IL-3 or interferon- gamma (IFN- gamma ).
USE - The compositions are used to treat or prevent infectious or other diseases, and to improve immune response (both systemic and local) to vaccination, in normal or immuno-compromised or immuno-suppressed subjects. They can also be used to optimise **monoclonal** **antibody** (MAb) production in vitro or in vivo, particularly for production of human MAbs.
NVA is used to neutralise cytokine(s) in situations where **antibody** production is pathogenic, e.g. in autoimmune diseases such as systemic lupus erythematosus, idiopathic thrombocytopaenic purpura, vasculitis, Grave's disease and allergy.
The compositions are administered, e.g. by injection, intranasally or orally. No dose is quoted.
ADVANTAGE - The composition leads to up to 100-fold increase in Ab secretion. The effects of GM-CSF and IL-3 are synergistic.
Dwg.3/13

L4 ANSWER 7 OF 34 CANCERLIT
ACCESSION NUMBER: 97621905 CANCERLIT
DOCUMENT NUMBER: 97621905
TITLE: Anti-idiotype-cytokine **fusion protein** for breast cancer therapy (Meeting abstract).
AUTHOR: Tripathi P K; Qin H-X; Xu; Foon K A; Bhattacharya-Chatterjee M; Chatterjee S K
CORPORATE SOURCE: Markey Cancer Center, University of Kentucky, Lexington, KY 40536.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1997). Vol. 38, pp. A563.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACT)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199711
AB We have generated a murine **monoclonal** anti-idiotype **antibody**, 11D10, which mimics biologically and antigenically a distinct and specific epitope of the high molecular weight human milk fat globule (HMFG). To augment the immunogenicity of 11D10 in vaccinated breast cancer patients, without using any carrier protein or **adjuvant**, we made a **chimeric** 11D10-GM-CSF **fusion protein** vaccine. An expression plasmid was made by ligation of the sequences of 11D10 light chain variable region, upstream of human kappa constant region. The heavy chain plasmid was made by ligation of the heavy chain variable region sequences upstream of human lambda1 constant region CH1 and DNA fragment encoding the mature GM-CSF peptide to the 3' to the CH3 exon. P3 plasmocytoma cells were transfected with the light and heavy chain vectors by electroporation. **Fusion protein** was purified from culture media by chromatography in protein A columns and was separated on 7.5% non-reducing and 12.5% reducing SDS-polyacrylamide gels for Western blotting. In non-reducing gel, a single band approx 180 kD reacted with anti-human kappa, anti-human lambda1 and anti-GM-CSF **antibodies**. In the reducing gel, a -74 kD protein reacted with anti-human lambda1 and anti-GM-CSF **antibodies**. The **fusion protein** induced proliferation of GM-CSF dependent NFS-60 cells and strongly bound to anti-HMFG **monoclonal** **antibody** (Ab1). These results suggest that the protein is a **chimeric** anti-idiotype **antibody** consisting of 11D10

variable domains, human kappa and lambda1 constant domains. GM-CSF molecule is fused to lambda1 and is biologically active.

L4 ANSWER 8 OF 34 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998020905 MEDLINE
DOCUMENT NUMBER: 98020905
TITLE: Bacterial lipopeptides constitute efficient novel immunogens and adjuvants in parenteral and oral immunization.
AUTHOR: Bessler W G; Baier W; v.d. Esche U; Hoffmann P; Heinevetter L; Wiesmuller K H; Jung G
CORPORATE SOURCE: Institut fur Immunbiologie der Universitat, Freiburg, Germany.
SOURCE: BEHRING INSTITUTE MITTEILUNGEN, (1997 Feb) (98) 390-9.
Ref: 32
Journal code: 9KJ. ISSN: 0301-0457.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104
AB Synthetic lipopeptide analogues derived from the N-terminus of bacterial lipoprotein constitute potent B-lymphocyte and **macrophage** /monocyte activators in vitro. In vivo they act as immunoadjuvants in parenteral and oral immunization when administered in combination with antigens. When added to bacterial or viral vaccines, lipopeptides markedly enhance the vaccine effect. After the coupling of lipopeptides to haptens or non immunogenic low molecular mass antigens, a specific **antibody** response is induced often after only one application of **the conjugate**. The response can be further enhanced by introducing haplotype specific T helper cell epitopes into the **conjugate**. Lipopeptide antigen conjugates can also be applied as synthetic vaccines that give protection e.g. against foot-and-mouth-disease. The novel chemically well defined lipopeptides described here can be synthesized in gram amounts with high purity and reproducibility; they are non-toxic and can be stored for long time even at room temperature. For veterinary application, by replacing Freund's **adjuvant**, side reactions and inflammatory processes are avoided.

L4 ANSWER 9 OF 34 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97254817 MEDLINE
DOCUMENT NUMBER: 97254817
TITLE: Genetically transferred central and peripheral immune tolerance via retroviral-mediated expression of immunogenic epitopes in hematopoietic progenitors or peripheral B lymphocytes.
AUTHOR: Zambidis E T; Kurup A; Scott D W
CORPORATE SOURCE: Department of Immunology, Holland Laboratory, American Red Cross, Rockville, Maryland 20855, USA.
CONTRACT NUMBER: AI29691 (NIAID)
T32-GM07356 (NIGMS)
T32-AI07285 (NIAID)
SOURCE: MOLECULAR MEDICINE, (1997 Mar) 3 (3) 212-24.
Journal code: CG3. ISSN: 1076-1551.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY WEEK: 19970904
AB BACKGROUND: Based on the hypothesis that IgGs are potent tolerogens and that immature lymphohematopoietic antigen-presenting cells (APC), and even mature peripheral B cells, may be effective APC for tolerance induction, we designed an immunoglobulin fusion protein retroviral expression vector to test the role of B cells in a novel gene therapy strategy for the transfer of immune tolerance. METHODS: An immunodominant epitope (residues 12-26 of the lambda repressor cI protein) was fused in frame to an IgG heavy chain in a retroviral vector, which was used to infect either bone marrow cells or activated peripheral B lymphocytes. These cells were transferred into syngeneic recipients, who were subsequently challenged with the 12-26 peptide in **adjuvant**. RESULTS: Bone marrow (BM) **chimeras** generated with retrovirally transduced bone marrow were shown to be profoundly unresponsive to the 12-26 peptide at both the humoral and cellular levels, but were competent to respond to an unrelated protein (lysozyme or PPD). Importantly, we also show that immunocompetent adult recipients infused with transduced mature, activated B lymphocytes, are rendered unresponsive by this treatment. Surprisingly, lymphoid-deficient BM progenitors from syngeneic SCID donors could also be transduced to produce tolerogenic **APC**. CONCLUSIONS: Our data suggest that activated B cells are sufficient to be effective tolerogenic **APC** in immunocompetent adult mice, but that nonlymphoid cells may also induce tolerance in reconstituted hosts. This approach for gene-transferred tolerogenesis has the potential to be maintained indefinitely, and it requires only knowledge of cDNA sequences of target antigens.

L4 ANSWER 10 OF 34 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 96:912023 SCISEARCH
THE GENUINE ARTICLE: VX026
TITLE: A nine-amino acid peptide from IL-1 beta augments antitumor immune responses induced by protein and DNA vaccines
AUTHOR: Hakim I; Levy S (Reprint); Levy R
CORPORATE SOURCE: STANFORD UNIV, MED CTR, DEPT MED, DIV ONCOL, STANFORD, CA 94305 (Reprint); STANFORD UNIV, MED CTR, DEPT MED, DIV ONCOL, STANFORD, CA 94305
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF IMMUNOLOGY, (15 DEC 1996) Vol. 157, No. 12, pp. 5503-5511.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 60
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB The idiotypic determinants of B cell lymphoma provide a tumor-specific Ag and a target for immunotherapy. We have developed several generations of idiotype vaccines that were tested in an animal model, the 38C13 mouse B cell lymphoma. Intitially we showed that effective tumor immunity was elicited by the syngeneic Id when it was conjugated to a carrier protein and mixed with an **adjuvant**, A subsequent generation of Id vaccines eliminated the need for a carrier protein and for an **adjuvant** by incorporating cytokines into fusion proteins containing the Id. A third generation of vaccines consisting of naked DNA encoding the Id-granulocyte-**macrophage** colony-stimulating factor (GM-CSF) fusion proteins was equally effective in inducing tumor immunity. To determine whether Ig variable regions,in the absence of constant regions, could be **immunotherapeutic** in this model, we tested the use of single-chain Fv (scFv), scFv proteins, produced in bacteria, and naked DNA encoding scFv were used in this study. scFv was tested alone or fused to CM-CSF or an immunoenhancing peptide derived from IL-1 beta. Here we demonstrate that scFv-CM-CSF was effective only when injected as a protein, not as a DNA vaccine. In contrast, both scFv-IL-1 beta peptide **fusion protein** and naked DNA encoding it induced tumor immunity that protected mice from tumor challenge.

L4 ANSWER 11 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96006656 EMBASE
DOCUMENT NUMBER: 1996006656
TITLE: **Monoclonal antibody** 7G3 recognizes the N-terminal domain of the human interleukin-3 (IL-3) receptor .alpha.-chain and functions as a specific IL-3 receptor antagonist.
AUTHOR: Sun Q.; Woodcock J.M.; Rapoport A.; Stomski F.C.; Korpelainen E.I.; Bagley C.J.; Goodall G.J.; Smith W.B.; Gamble J.R.; Vadas M.A.; Lopez A.F.
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Inst. of Medical/Veterinary Science, Frome Road,Adelaide, SA 5000, Australia
SOURCE: Blood, (1996) 87/1 (83-92).
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The human interleukin-3 receptor (IL-3R) is expressed on myeloid, lymphoid, and vascular endothelial cells, where it transduces IL-3-dependent signals leading to cell activation. Although IL-3R activation may play a role in hematopoiesis and immunity, its aberrant expression or excessive stimulation may contribute to pathologic conditions such as leukemia, lymphoma, and allergic reactions. We describe here the generation and characterization of a **monoclonal antibody** (MoAb), 7G3, which specifically binds to the IL-3R .alpha.-chain and completely abolishes its function. MoAb 7G3 immunoprecipitated and recognized in Western blots the IL-3R .alpha.-chain expressed by transfected cells and bound to primary cells expressing IL-3R.alpha.. MoAb 7G3 bound the IL-3R .alpha.-chain with a k(d) of 900 pmol/L and inhibited 125I-IL-3 binding to high- and low-affinity receptors in a dose- dependent manner. Conversely, IL-3 but not granulocyte-**macrophage** colony- stimulating factor (GM-CSF) inhibited 125I-7G3 binding to high- and low- affinity IL-3Rs, indicating that MoAb 7G3 and IL-3 bind to common or adjacent sites. In keeping with the inhibition of IL-3 binding, MoAb 7G3 antagonized IL-3 biologic activities, namely stimulation of TF-1 cell proliferation, basophil histamine release, and IL-6 and IL-8 secretion from human endothelial cells. Two other anti-IL-3R .alpha.-chain MoAbs failed to inhibit IL- 3 binding or function. Epitope mapping experiments using truncated IL-3R .alpha.- chain mutants and IL-3R.alpha./GM-CSFR.alpha. **chimeras** revealed that 31 amino acids in the N-terminus of IL-3R.alpha. were required for MoAb 7G3 binding. MoAb 7G3 may be of clinical significance for antagonizing IL-3 in pathologic conditions such as some myeloid leukemias, follicular B-cell lymphoma, and allergy. Furthermore, these results implicate the N-terminal domain of IL-3R.alpha. in IL- 3 binding. Since this domain is unique to the IL-3/GM-CSF/IL-5 receptor subfamily, it may represent a novel and common binding feature in these receptors.

L4 ANSWER 12 OF 34 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 95-215041 [28] WPIDS
CROSS REFERENCE: 95-194032 [25]
DOC. NO. CPI: C95-099408
TITLE: Stimulating **antibody** prodn. by B cells using interleukin 3 - or granulocyte **macrophage** colony stimulating factor, partic. useful as vaccine **adjuvant**, also neutralising **adjuvant** to inhibit pathogen in **antibody** prodn..
DERWENT CLASS: B04 D16
INVENTOR(S): MOND, J J; SNAPPER, C M
PATENT ASSIGNEE(S): (MOND-I) MOND J J; (SNAP-I) SNAPPER C M; (USSA) US SEC OF ARMY; (JACK-N) JACKSON FOUND ADVANCEMENT MILITARY MED
COUNTRY COUNT: 20
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9513089 | A1 | 950518 | (9528)* | EN | 52 |
| RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE | | | | | |
| W: AU CA JP | | | | | |
| AU 9510511 | A | 950529 | (9537) | | |
| EP 728013 | A1 | 960828 | (9639) | EN | |
| R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| JP 09507055 | W | 970715 | (9738) | | 48 |
| AU 699913 | B | 981217 | (9911) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|

| | |
|---|---|
| WO 9513089 A1 | WO 94-US12802 941108 |
| AU 9510511 A | AU 95-10511 941108 |
| EP 728013 A1 | WO 94-US12802 941108 |
| | EP 95-901168 941108 |
| JP 09507055 W | WO 94-US12802 941108 |
| | JP 95-513925 941108 |
| AU 699913 B | AU 95-10511 941108 |

FILING DETAILS:

| PATENT NO KIND | PATENT NO |
|---|---|
| AU 9510511 A Based on | WO 9513089 |
| EP 728013 A1 Based on | WO 9513089 |
| JP 09507055 W Based on | WO 9513089 |
| AU 699913 B Previous Publ. | AU 9510511 |
| Based on | WO 9513089 |

PRIORITY APPLN. INFO: US 94-315492 940930; US 93-150510 931110

AB WO 9513089 A UPAB: 950721

Compsn. for stimulating release of **antibodies** (Ab) by B cells comprises granulocyte-**macrophage** colony stimulating factor (GM-CSF) and/or interleukin-3 (IL-3). Also claimed are: (1) vaccine **adjuvant** contg. GM-CSF and/or IL-3 bound covalently to a multivalent carrier (MVC); (2) **conjugate** vaccine contg. this **adjuvant** and an antigen (Ag), also bound covalently to MVC; (3) neutralising vaccine **adjuvant** consisting of separate **antibodies** against GM-CSF, IL-3 and gamma-interferon (IFNg); (4) in vitro assay system for identifying compsns. useful for stimulating release of Ab comprising anti-IgD or IgM/dextran **conjugate** plus highly purified B cells.

USE - The compsn. is used to optimise in vivo or in vitro prodn. of Ab against Ag, partic. to improve response to vaccination in mammals, under either normal or immunodepressed/ immunocompromised conditions. The neutralising **adjuvant** is used to treat autoimmune diseases (i.e. to suppress prodn. of pathogen **antibodies**) e.g. systemic lupus erythematosus, vasculitis, Graves' disease, allergy, etc. No dosage given. The compsns. are administered by injection, intranasally, intravaginally or orally.

ADVANTAGE - The compsns. increase Ab prodn. both systemically and locally, e.g. when Gm-CSF and IL-3 are used together they act synergistically to provide a 100-fold increase, and this is improved further by admin. of IFNg. In the assay system, use of highly purified B cells avoids problems of stimulatory cytokines produced by contaminating cells.

Dwg.2/6

L4 ANSWER 13 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95099946 EMBASE
DOCUMENT NUMBER: 1995099946
TITLE: Induction of autoantibody responses to GM-CSF by hyperimmunization with an Id-GM-CSF **fusion protein**.
AUTHOR: Chen T.T.; Levy R.
CORPORATE SOURCE: Division of Oncology, Department of Medicine, Stanford University Medical Center,Stanford, CA 94305, United States
SOURCE: Journal of Immunology, (1995) 154/7 (3105-3117).
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Fusion proteins consisting of an Ig containing xenogeneic constant regions and granulocyte-**macrophage** colony-stimulating factor (Id-GM-CSF) are potent immunogens capable of inducing anti-idiotypic Abs after two immunizations, without the usual need for adjuvants or carrier proteins. In this study, we investigated the effects of hyperimmunization with Id-GM-CSF and found that it induces anti-GM-CSF Abs that could bind to GM-CSF and neutralize its bioactivity in vitro. However, no detrimental effects of the anti-GM-CSF activity were apparent on the general health of the animals or on their base line white blood cell counts. Mice with the anti-GM-CSF activity reconstituted their peripheral white blood cells with identical kinetics as control mice after high dose cyclophosphamide treatment, sublethal irradiation, or lethal irradiation followed by syngeneic bone marrow transplantation. Primary and secondary Ab responses to a variety of protein Ags, including an unrelated Ig Id, were not affected. However, the anti-Id response induced by an unrelated GM-CSF **fusion protein** that is dependent upon the GM-CSF bioactivity was impaired. To avoid any potential problems associated with inducing anti-GM-CSF Abs, we show that priming with the Id- GM-CSF protein and boosting with the Id protein alone were sufficient to induce comparable anti-Id titers without inducing anti-GM-CSF Abs. We conclude that although hyperimmunization of mice with the GM-CSF **fusion protein** induced neutralizing anti-GM-CSF Abs, this was of little consequence to the animals. Nevertheless, we have devised a strategy to overcome this potential limitation on the use of GM-CSF fusion proteins for immunization.

L4 ANSWER 14 OF 34 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 95:44518 SCISEARCH
THE GENUINE ARTICLE: PZ135
TITLE: INHIBITION OF HEPATIC METASTASES OF HUMAN COLON-CANCER IN NUDE-MICE BY A **CHIMERIC** SF-25 **MONOCLONAL -ANTIBODY**
AUTHOR: TAKAHASHI H (Reprint); NAKADA T; NAKAKI M; WANDS J R
CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, GASTROINTESTINAL UNIT, JACKSON 7, FRUIT ST, BOSTON, MA, 02114 (Reprint); HARVARD UNIV, SCH MED, DEPT MED, BOSTON, MA, 00000; MASSACHUSETTS GEN HOSP, CTR CANC, MOLEC HEPATOL LAB, BOSTON, MA, 00000
COUNTRY OF AUTHOR: USA
SOURCE: GASTROENTEROLOGY, (JAN 1995) Vol. 108, No. 1, pp. 172-182.
ISSN: 0016-5085.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 45
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background/Aims: Hepatic metastasis is one of the most serious complications of human colon cancer. A murine-human **chimeric** SF-25 **monoclonal antibody** was prepared, and this construct recognizes a cell surface antigen highly present in human colon adenocarcinoma. Methods: This study determined if the **chimeric** SF-25 **monoclonal antibody** inhibits the outgrowth of hepatic metastases of human colon adenocarcinoma using an athymic nude mouse model. Results: A single intravenous injection of **chimeric** SF-25 **monoclonal antibody** significantly inhibited the outgrowth of 5 and 7-day hepatic micrometastases (P = 0.0001 and 0.004, respectively, vs. untreated) and improved the survival of the animals. No detectable tumor was found in the liver when mice were treated by multiple injections of the **antibody** immediately after tumor cell grafting into the portal vein. In contrast, F(ab')(2) fragments did not show antitumor effects, and the administration of natural killer cell or **macrophage** depleting agents (anti-asialo GM1 **antibody** and carrageenan, respectively) substantially inhibited the antitumor effects of **chimeric** SF-25 **monoclonal antibody** in vivo. Conclusions: **Chimeric** SF-25 **monoclonal antibody** inhibits growth of hepatic metastasis of human colon cancer, and cell-mediated host immune mechanisms seem to be important for its in vivo antitumor activity.

L4 ANSWER 15 OF 34 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 95193317 MEDLINE
DOCUMENT NUMBER: 95193317
TITLE: **Adjuvant** Quil A improves protection in mice and enhances opsonic capacity of antisera induced by pneumococcal polysaccharide **conjugate** vaccines.
AUTHOR: DeVelasco E A; Dekker H A; Antal P; Jalink K P; van Strijp J A; Verheul A F; Verhoef J; Snippe H
CORPORATE SOURCE: Eijkman-Winkler Institute of Medical Microbiology, Utrecht University, The Netherlands..
SOURCE: VACCINE, (1994 Nov) 12 (15) 1419-22.
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506

AB The **adjuvant** effect of Quil A on the primary **antibody** response of mice to pneumococcal capsular polysaccharide conjugates was examined. Quil A increased the anti-capsular polysaccharide **antibody** titres, the protection against Streptococcus pneumoniae, and the opsonic capacity of the **antibodies** as measured in a newly developed in vitro phagocytosis assay, using the mouse **macrophage** cell line J774.

L4 ANSWER 16 OF 34 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 94:311569 SCISEARCH
THE GENUINE ARTICLE: NL649
TITLE: INTERFERON-GAMMA-PRODUCING AND INTERLEUKIN-4-PRODUCING T-CELLS CAN BE PRIMED ON DENDRITIC CELLS IN-VIVO AND DO NOT REQUIRE THE PRESENCE OF B-CELLS
AUTHOR: RONCHESE F (Reprint); HAUSMANN B; LEGROS G
CORPORATE SOURCE: MALAGHAN INST MED RES, POB 7060, WELLINGTON, NEW ZEALAND (Reprint); BASEL INST IMMUNOL, BASEL, SWITZERLAND; CIBA GEIGY CORP, DEPT ALLERGY IMMUNOL, BASEL, SWITZERLAND
COUNTRY OF AUTHOR: NEW ZEALAND; SWITZERLAND
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (MAY 1994) Vol. 24, No. 5, pp. 1148-1154.
ISSN: 0014-2980.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 43
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The antigen-presenting cell (**APC**) requirements for the in vivo induction of Th1 and Th2-type responses were investigated using a severe combined immunodeficiency (SCID)mouse **chimera** model. SCID mice adoptively transferred with either T cells [SCID(T)] or T + B cells [SCID(T + B)] and immunized with antigen in **adjuvant** were able to generate antigen-specific T cells which could produce both interferon (IFN)-gamma and interleukin (IL)-4 upon in vitro restimulation. This suggests that B cell **APC** are not necessary for the priming of either IFN-gamma- or IL-4-producing T cells in vivo. The ability of different **APC** to activate Th2-dependent effector mechanisms was also investigated. SCID(T) and SCID(T + B) mice were infected with the nematode parasite Nippostrongylus brasiliensis and analyzed for the development of IL-5-dependent peripheral blood eosinophilia. Following infection both SCID(T) and SCID(T + B) mice generated similar numbers of peripheral blood eosilnophils, suggesting that similar amounts of IL-5 had been produced. Therefore, B cell **APC** are also not required for the in vivo activation of Th2 cells to lymphokine production. To establish more precisely which **APC** prime T cells to produce IFN-gamma and IL-4, normal mice were immunized by injection of syngeneic splenic dendritic cells which had been pulsed with antigen in vitro. T cells from these immunized mice were able to produce good IFN-gamma and IL-4 responses upon in vitro restimulation with specific antigen; therefore, dendritic cells appear to be sufficient **APC** for the in vivo priming of both IFN-gamma- and IL-4-producing T cells.

L4 ANSWER 17 OF 34 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95180241 MEDLINE
DOCUMENT NUMBER: 95180241
TITLE: Potential role of granulocyte-**macrophage**

colony-stimulating factor as vaccine **adjuvant**.
AUTHOR: Jones T; Stern A; Lin R
CORPORATE SOURCE: Clinical Research, Sandoz Pharma Ltd, Basel, Switzerland..
SOURCE: EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY AND INFECTIOUS
DISEASES, (1994) 13 Suppl 2 S47-53. Ref: 23
Journal code: EM5. ISSN: 0934-9723.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
AB The uses of GM-CSF as an immunomodulator and vaccine **adjuvant** are reviewed. GM-CSF has a variety of effects on immune responses: it induces class II major histocompatibility complex antigen expression on the surface of macrophages; it enhances **dendritic cell** maturation and migration; it results in a localized inflammation at the injection site; and it has marked effects on maturation of haematopoietic progenitor cells in the bone marrow. Animal and human studies suggest that administration of GM-CSF can increase **antibody** titres to foreign antigens. Monkeys injected with human interleukin (IL)-3 plus GM-CSF, at a different injection site, developed peak **antibody** titres which were 8- to 30-fold higher than those in monkeys injected with IL-3 alone. In a study of ovarian cancer patients receiving GM-CSF to prevent chemotherapy-induced neutropenia, two patients who had demonstrated a low titre of antithyroid **antibodies** prior to the study showed an increase in **antibody** titre and transient thyroiditis after administration of GM-CSF. Recently a GM-CSF/antigen **fusion protein** has been tested. An **antibody** corresponding to a specific idiotype expressed on B-cell lymphomas was fused to GM-CSF and injected into mice with B-cell lymphoma xenografts. The mice developed **antibodies** to the lymphoma and there was a protective effect against disease progression. Preliminary results of clinical trials using GM-CSF in humans suggest that it enhances **antibody** responses to hepatitis B vaccine. On the basis of these preliminary results, several clinical trials are being planned and it would appear that GM-CSF has potential as a vaccine **adjuvant**.

L4 ANSWER 18 OF 34 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 93226047 MEDLINE
DOCUMENT NUMBER: 93226047
TITLE: Idiotype/granulocyte-**macrophage** colony-stimulating factor **fusion protein** as a vaccine for B-cell lymphoma [see comments].
COMMENT: Comment in: Nature 1993 Apr 22;362(6422):695
Comment in: Nature 1993 Aug 5;364(6437):493
AUTHOR: Tao M H; Levy R
CORPORATE SOURCE: Department of Medicine, School of Medicine, Stanford University, California 94305.
SOURCE: NATURE, (1993 Apr 22) 362 (6422) 755-8.
Journal code: NSC. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199307
AB To produce a vaccine against cancer, antigens must be found that are preferentially expressed by tumour cells and can induce an immune response against the tumour. The variable regions of the immunoglobulin molecules expressed on malignant B cells (idiotypes) are tumour-specific, but are weak immunogens. To induce an immune response in animals or humans, the idiotypic protein has therefore to be chemically coupled to a strongly immunogenic protein and mixed with an **adjuvant**. The resulting response can protect animals from subsequent tumour challenge, and cure animals with established tumours in combination with chemotherapy. Granulocyte-**macrophage** colony-stimulating factor (GM-CSF) augments antigen presentation in a variety of cells. Here we show that by fusing a tumour-derived idiotype to GM-CSF, it can be converted into a strong immunogen capable of inducing idiotype-specific **antibodies** without other carrier proteins or adjuvants and of protecting recipient animals from challenge with an otherwise lethal dose of tumour cells. This approach may be applicable to the design of vaccines for a variety of other diseases.

L4 ANSWER 19 OF 34 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 93380027 MEDLINE
DOCUMENT NUMBER: 93380027
TITLE: Immunotargeting of thyroglobulin on antigen presenting cells abrogates natural tolerance in the absence of **adjuvant**.
AUTHOR: Balasa B; Carayanniotis G
CORPORATE SOURCE: Division of Endocrinology, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Canada..
SOURCE: CELLULAR IMMUNOLOGY, (1993 Sep) 150 (2) 453-8.
Journal code: CQ9. ISSN: 0008-8749.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199312
AB Mice usually develop strong IgG responses to self-thyroglobulin (Tg) following immunization with mouse Tg (mTg) emulsified in complete Freund's **adjuvant** (CFA). Here we report that **adjuvant**-free challenge of mice with small doses of mTg conjugated onto a **monoclonal antibody** (MAb) specific for class II MHC determinants (anti-I-Ak) induces an mTg-specific IgG response in CBA (H-2k) but not in B6 (H-2b) mice. This is not a result of nonspecific uptake of immunoconjugate or chemical modification of mTg because mTg conjugated in a similar manner to a control MAb (specific for influenza nucleoprotein) of the same IgG subclass as the anti-I-Ak MAb did not elicit an autoimmune response. Despite the presence of mTg-specific IgG with titers equal to those observed after challenge with mTg in CFA, thyroid lesions were not detected in CBA mice that received mTg-(anti-I-Ak Mab) **conjugate** indicating a clear divergence in the requirements for autoantibody production and disease. The data suggest that small amounts of soluble autoantigen, conjugated onto MAbs specific for determinants expressed on antigen-presenting cells (**APC**), can effectively abrogate natural tolerance perhaps via a targeting mechanism that focuses autoantigen on **APC**. This approach may help elucidate the role of various **APC** subsets in autoimmunity and allow the study of initial events that trigger autoreactivity outside a CFA-induced granuloma site.

L4 ANSWER 20 OF 34 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 93094593 MEDLINE
DOCUMENT NUMBER: 93094593
TITLE: Effect of Haemophilus influenzae polysaccharide,outer membrane protein complex **conjugate** vaccine on macrophages.
AUTHOR: Ambrosino D M; Bolon D; Collard H; Van Etten R; Kanchana M V; Finberg R W
CORPORATE SOURCE: Laboratory of Infectious Diseases, Dana-Farber Cancer Institute, Boston, MA 02115.
CONTRACT NUMBER: AI29623 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1992 Dec 15) 149 (12) 3978-83.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199303
AB Haemophilus influenzae type b polysaccharide-**conjugate** vaccines elicit protective **antibody** responses in young infants. One of these conjugates, polysaccharide linked to outer membrane protein complex (PRP-OMPC), is produced by linking the capsular polysaccharide to an outer membrane protein complex derived from group B Neisseria meningitidis. The outer membrane protein complex contains T cell carrier epitopes that elicit T cell-dependent **antibody** responses. OMPC also has been shown to increase the **antibody** response to other proteins administered concurrently that are not covalently linked (i.e., acts as an **adjuvant**). In this study PRP-OMPC immunized mice demonstrated significant increases in spleen size as well as in splenocyte number as compared to saline controls ($p < 0.01$, $p < 0.001$, respectively). No such increase was noted after immunization with another H. influenzae type b-**conjugate** vaccine, oligosaccharide linked to a variant of diphtheria toxin. By analytic flow cytometry, the mice immunized with PRP-OMPC demonstrated an increase in large splenocytes expressing the Ag Mac-1 (CD11b, CR3). Furthermore, the spleens on histologic examination were characterized by an increase in the red pulp area consisting predominantly of cells of **macrophage** morphology. By immunohistochemical staining, the cells were identified as macrophages due to expression of Mac-1 and p150,95 (CD11C) Ag. After PRP-OMPC immunization, severe combined immunodeficient mice also demonstrated significant splenomegaly with an increase in macrophages identified by expression of Mac-1 and MHC class II Ag. Thus PRP-OMPC vaccine resulted in T cell-independent splenomegaly with an increase number of macrophages. We propose that this unique property may confer increased immunogenicity to PRP-OMPC through **macrophage** activation and cytokine release. Furthermore, the effect on macrophages may explain the "**adjuvant** " capacity of OMPC.

L4 ANSWER 21 OF 34 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 92:225885 SCISEARCH
THE GENUINE ARTICLE: HL948
TITLE: ACTIVATION OF MOUSE MACROPHAGES BY MURAMYL DIPEPTIDE COUPLED WITH AN ANTIMACROPHAGE **MONOCLONAL-ANTIBODY**
AUTHOR: MIDOUX P; MARTIN A; COLLET B; MONSIGNY M; ROCHE A C; TOUJAS L (Reprint)
CORPORATE SOURCE: CTR REG LUTTE CONTRE CANC, SERV IMMUNOL IMMUNOTHERAPIE, F-35033 RENNES, FRANCE; CNRS, INSERM, CTR BIOPHYS MOLEC, DEPT BIOCHIM GLYCOCONJUGUES & LECTINES ENDOGENES, F-45045 ORLEANS, FRANCE; UNIV ORLEANS, F-45071 ORLEANS 2, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: BIOCONJUGATE CHEMISTRY, (MAR/APR 1992) Vol. 3, No. 2, pp. 194-199.
ISSN: 1043-1802.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 50
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB A rat IgG2a **monoclonal antibody** (mAb3A33) directed against the mouse Mac-1 antigen was conjugated with muramyl dipeptide (MDP) by using an intermediate polymer; under such conditions 75 MDP molecules were bound to one **antibody** molecule. A poly(L-lysine) polymer substituted with muramyl dipeptide and 3-(2-pyridyldithio)propionyl residues was prepared, the remaining lysine epsilon-amino groups were acylated with D-gluconolactone, leading to a neutral polymer; then a few polymer conjugates were coupled to mAb3A33 via a disulfide bridge. The binding capacity of the **monoclonal antibody** was preserved after conjugation with MDP-polymer molecules. Mouse peritoneal macrophages, incubated for 24 h with MDP-mAb3A33 **conjugate** became cytostatic against P815 mastocytoma cells, whereas unconjugated mAb3A33 and MDP-bound to a nonspecific rat IgG2a were ineffective. An enhancement of the cytostatic activity induced by MDP-mAb3A33 **conjugate** was obtained in the presence of gamma-IFN. These results show that several tens of MDP molecules can be

linked to a **macrophage**-specific **monoclonal antibody** by using a neutral intermediate polymer without impairing the binding **antibody** capacity and that this type of MDP **conjugate** can efficiently activate macrophages and therefore could be the basis of the development of new antitumor therapy.

L4 ANSWER 22 OF 34 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 92008132 MEDLINE
DOCUMENT NUMBER: 92008132
TITLE: Mycobacterial heat-shock proteins as carrier molecules.
AUTHOR: Lussow A R; Barrios C; van Embden J; Van der Zee R; Verdini A S; Pessi A; Louis J A; Lambert P H; Del Giudice G
CORPORATE SOURCE: World Health Organization-Immunology Research and Training Center, Department of Pathology, University of Geneva, Switzerland..
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Oct) 21 (10) 2297-302.
Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199201
AB We have previously shown that the priming of mice with live Mycobacterium tuberculosis var. bovis (Bacillus Calmette-Guerin, BCG) and immunization with the repetitive malaria synthetic peptide (NANP)40 conjugated to purified protein derivative (PPD), led to the induction of high and long-lasting titers of anti-peptide IgG **antibodies**, overcoming the requirement of adjuvants and the genetic restriction of the **antibody** response to the peptide (Lussow et al., Proc. Natl. Acad. Sci. USA 1990. 87:2960). This initial work led us to the following observations. BCG had to be live for priming to lead to the induction of anti-peptide **antibodies**. Surprisingly, priming with other living microorganisms which chronically infect the **macrophage** (e.g. Salmonella typhimurium and Leishmania major) also induced anti-peptide **antibodies** in mice immunized with PPD-(NANP)40 **conjugate**. It was, thus, hypothesized that molecules expressed during active infection and also known to be highly conserved between species, namely the heat-shock proteins (hsp), could mediate the T cell sensitization required for the production of anti-peptide **antibodies**. In fact, when the PPD protion of the **conjugate** was replaced by a highly purified recombinant protein corresponding to the 65-kDa (GroEL-type) hsp of M. bovis, this resulted in the production of anti-(NANP) IgG **antibodies** in BCG-primed mice, irrespective of the major histocompatibility complex-controlled responsiveness to the (NANP) sequence itself. Further, similar induction of anti-peptide **antibody** response was also obtained with a recombinant 70-kDa (DnaK-type) hsp of M. tuberculosis, but not with a small molecular mass (18 kDa) of M. leprae. Finally, an adjuvant-free carrier effect for anti-peptide IgG **antibody** production in BCG-primed mice, was also exerted by the GroEL hsp of Escherichia coli. This finding that hsp can act as carrier molecules without requiring conventional adjuvants is of potential importance in the development of vaccine strategies.

L4 ANSWER 23 OF 34 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 92039819 MEDLINE
DOCUMENT NUMBER: 92039819
TITLE: The generation of **antibody** in mice to tuftsin: a naturally occurring phagocytosis stimulating tetrapeptide.
AUTHOR: Naim J O; van Oss C J
CORPORATE SOURCE: Department of Surgery, Rochester General Hospital, New York 14621..
SOURCE: IMMUNOLOGICAL INVESTIGATIONS, (1991 Jul) 20 (4) 351-64.
Journal code: GI5. ISSN: 0882-0139.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
AB Tuftsin (Thr-Lys-Pro-Arg) is a naturally occurring tetrapeptide that stimulates most known functions of the polymorphonuclear leukocyte and **macrophage** cell lines. We previously reported our unsuccessful attempts to generate antituftsin **antibodies** by conjugating tuftsin to several carrier proteins and by polymerizing the peptide with glutaraldehyde. To render tuftsin antigenic the following modifications were made to native tuftsin: three glycine residues were added to the N terminus of tuftsin (Gly3-tuf) and cysteine was added to the N terminus (Cys-tuf) and to the C terminus (tuf-Cys). Native tuftsin was covalently conjugated to sheep red blood cells (SRBC). In a separate experiment Balb/c mice primed with SRBC were immunized with 10(7) SRBC peptide **conjugate**. Native tuftsin and Gly3-tuf were also conjugated to keyhole limpet hemocyanin (KLH). In another experiment KLH and cationized bovine serum albumin (cBSA) were activated with sulfo-succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (s-SMCC), which was used to control orientation of tuf-Cys and Cys-tuf when conjugated to each carrier protein. All conjugates were administered in complete Freund's **adjuvant** (CFA) except for cBSA conjugates which were administered in alum. **Antibody** response was determined by solid phase radioimmunoassay. Results showed that specific antituftsin **antibodies** were elicited only by Cys-tuf, conjugated to KLH. This study reaffirms that tuftsin is weakly antigenic and confirms the previous work by Gottlieb et al. that **antibody** to tuftsin can only be elicited when tuftsin is conjugated to the carrier protein KLH in a manner that leaves the peptide carboxyl end free.

L4 ANSWER 24 OF 34 MEDLINE
ACCESSION NUMBER: 91278754 MEDLINE
DOCUMENT NUMBER: 91278754
TITLE: Ia restriction specificity of KLH-specific T cells from allogeneic bone marrow **chimeras** is influenced by histocompatibility at the H-2 and minor histocompatibility loci.
AUTHOR: Ogasawara K; Fukushi N; Mishima M; Good R A; Onoe K
CORPORATE SOURCE: Section of Pathology, Hokkaido University..
CONTRACT NUMBER: AG05628 (NIA)
AI22360 (NIAID)
SOURCE: MICROBIOLOGY AND IMMUNOLOGY, (1990) 34 (12) 1025-39.
Journal code: MX7. ISSN: 0385-5600.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
AB Ia restriction specificity involved in T cell proliferative responses to keyhole limpet hemocyanin (KLH) has been analyzed using a variety of allogeneic bone marrow **chimeras**. The **chimeric** mice were prepared by reconstituting irradiated AKR, SJL, B10.BR and B10.A(4R) mice with bone marrow cells from B10 mice. When such **chimeric** mice had first been primed with KLH in complete Freund's **adjuvant** (CFA), T cells from H-2 incompatible fully allogeneic **chimeras** showed significantly higher responses to KLH in the presence of antigen-presenting cells (**APC**) of donor strain (B10) than **APC** of recipient strain. However, in H-2 subregion compatible **chimeras**, [B10----B10.A(4R)], which were matched at the H-2D locus and at minor histocompatible loci, the T cells could mount vigorous responses to KLH with antigen-presenting cells (**APC**) of either donor or recipient type. The same results were obtained as well with **chimeras** that had been thymectomized after full reconstitution of lymphoid tissues by donor-derived cells. A considerable proportion of KLH-specific T cell hybridomas established from [B10----B10.A(4R)] **chimeras** exhibited both I-Ab and I-Ak restriction specificities. The present findings indicate that the bias to donor Ia type of antigen specific T cells is determined by donor-derived **APC** present in the extrathymic environment but that cross-reactivity to the recipient Ia is influenced to some degree by histocompatibility between donor and recipient mice, even though the histocompatible H-2D locus and minor histocompatibility loci seem not to be directly involved in the I-A restricted responses studied herein.

L4 ANSWER 25 OF 34 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 90125241 MEDLINE
DOCUMENT NUMBER: 90125241
TITLE: Specific **antibody** response towards predicted epitopes of the epidermal growth factor receptor induced by a thermostable synthetic peptide **adjuvant conjugate**.
AUTHOR: Muller C P; Buhring H J; Becker G; Jung C C; Jung G; Troger W; Saalmuller A; Wiesmuller K H; Bessler W G
CORPORATE SOURCE: Medizinische Universitatsklinik, Universitat Tubingen, FRG..
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1989 Dec) 78 (3) 499-504.
Journal code: DD7. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199005
AB Applying computer-assisted epitope prediction to the amino-acid sequence of the epidermal growth factor receptor (EGFR), the extracytoplasmic domain EGFR(516-529) was selected as a putative antigenic region. EGFR(516-529) was synthesized on a solid-phase matrix and N-terminally linked to the low mol. wt **adjuvant** tripalmitoyl-S-glyceryl-cysteinyl-serine (Pam3 Cys-Ser). The conjugation to this B cell and **macrophage**-activating lipopeptide considerably enhanced the immunogenicity of the EGFR peptide. Using the **conjugate** Pam3 Cys-Ser-EGFR(516-529), a peptide-specific **monoclonal antibody** was produced. By flow cytometry and immunoprecipitation the **antibody** was demonstrated to recognize EGFR on A431 cells, expressing large numbers of EGFR. With this novel approach synthetic immunogens can be prepared which could serve as thermostable synthetic vaccines with great potential in countries where a functional cold chain cannot be maintained.

L4 ANSWER 26 OF 34 MEDLINE
ACCESSION NUMBER: 89247776 MEDLINE
DOCUMENT NUMBER: 89247776
TITLE: Molecular dynamics of the alpha-helical epitope of a novel synthetic lipopeptide foot-and-mouth disease virus vaccine.
AUTHOR: Krug M; Folkers G; Haas B; Hess G; Wiesmuller K H; Freund S; Jung G
SOURCE: BIOPOLYMERS, (1989 Jan) 28 (1) 499-512.
Journal code: A5Z. ISSN: 0006-3525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 198909
AB A novel synthetic foot-and-mouth disease virus (FMDV) peptide vaccine consisting of a synthetic B-cell and **macrophage** activator covalently linked to an amphiphilic alpha-helical T-cell epitope was developed. The low molecular weight vaccine of 3400 daltons is composed of virus VP1 antigenic determinant and the immunologically active lipotripeptide tripalmitoyl-S-glyceryl-cysteinyl-seryl-serine (P3CSS) as built-in **adjuvant**. The vaccine, tripalmitoyl-S-glyceryl-cysteinyl-seryl-seryl-FMDV-VP1 (VP1 = serotype O1K 135-154) induces protection against homologous challenge and serotype-specific virus neutralizing **antibodies** in guinea pigs after single administration without further adjuvants or carriers. A P3CSS **conjugate** with the FMDV-VP1 segment 135-154 of strain O Wuppertal produced only poor cross-protection against challenge with O1K virus. The antigenic determinant VP1(135-154) is an amphiphilic alpha-helix, as shown by CD. Molecular dynamics simulations (MDS) carried out using the highly homologous alpha-helical alcohol dehydrogenase (ADH) segment H3 as starting conformation for VP1(138-149) suggest that the FMDV segment 138-149 may adopt alpha-helical conformation during binding to its T-cell receptor, and that the development of the system during MDS may be considered as the dissociation step of the complex.

L4 ANSWER 27 OF 34 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 87-315239 [45] WPIDS
DOC. NO. CPI: C87-134055

09/007,093

TITLE: New antigen-antibody conjugate - useful as vaccine in which antibody acts as delivery vehicle for targetting foreign antigens onto recipient cells.
DERWENT CLASS: B04 D16
INVENTOR(S): BARBER, B H; CARAYANNIOTIS, G; CARAYANNOT, G; CARAYANNOTIS, G
PATENT ASSIGNEE(S): (CONN-N) CONNAUGHT LAB LTD
COUNTRY COUNT: 18
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| EP 245078 | A | 871111 (8745)* | | EN | 12 |
| R: AT BE CH DE ES FR GB GR IT LI LU NL SE | | | | | |
| JP 63045228 | A | 880226 (8814) | | | |
| US 4950480 | A | 900821 (9036) | | | |
| EP 245078 | B | 911227 (9201) | | | |
| R: AT BE CH DE ES FR GB GR IT LI LU NL SE | | | | | |
| DE 3775458 | G | 920206 (9207) | | | |
| US 5194254 | A | 930316 (9313) | | | |
| CA 1327523 | C | 940308 (9415) | | | |
| JP 06074210 | B2 | 940921 (9436) | | | 9 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| EP 245078 | A | EP 87-304005 | 870505 |
| JP 63045228 | A | JP 87-110400 | 870506 |
| US 4950480 | A | US 87-46095 | 870505 |
| US 5194254 | A CIP of | US 87-46095 | 870505 |
| | | US 89-421188 | 891013 |
| CA 1327523 | C | CA 87-536274 | 870504 |
| JP 06074210 | B2 | JP 87-110400 | 870506 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| US 5194254 | A CIP of | US 4950480 |
| JP 06074210 | B2 Based on | JP 63045228 |

PRIORITY APPLN. INFO: GB 86-10983 860506; US 89-421188 891013
AB EP 245078 A UPAB: 930922
Novel conjugate (I), suitable for admin to a mammal to elicit an immune response, comprises an antigen conjugated with a monoclonal antibody specific for a surface structure of antigen-presenting cells
USE/ADVANTAGE - (I) may be used as a vaccine to elicit an IgG antibody response to an antigen. This it achieves without an immunogenicity-enhancing adjuvant. Thus use of (I) is a mcumuch safer method of enhancing the immunogenicity of weak antigens, and may be
employed for materials which are not normally very antigenic, e.g. small peptides, which are epitopes of larger proteins or are protein subunits of the pathogens themselves. The use of such epitopes or protein subunits in the form of conjugates with targeting monoclonal antibodies, as a vaccination method, avoids injection of killed or attenuated organisms with concurrent side-effects.
0/0

L4 ANSWER 28 OF 34 MEDLINE
ACCESSION NUMBER: 84184754 MEDLINE
DOCUMENT NUMBER: 84184754
TITLE: Immunogenicity of a hapten-carrier conjugate taken up by peritoneal cells.
AUTHOR: Neveu P J
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1984) 74 (2) 126-31.
Journal code: GP9. ISSN: 0020-5915.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198408
AB The present experiments have been performed in order to study the immunogenicity of antigen taken up by peritoneal macrophages using the hapten-carrier model and to investigate the role of macrophages in the antigenic competition between hapten and carrier moieties of the antigen molecule we have previously described. Guinea pigs were immunized with peritoneal cells collected from guinea pigs previously injected intraperitoneally with soluble or glutaraldehyde-polymerized hapten-carrier conjugates in Freund's incomplete adjuvant. Delayed hypersensitivity reactions to the carrier and anaphylactic reactions to both the hapten and the carrier were studied 14 and 16 days after immunization. After immunization with macrophage -associated hapten-carrier conjugate, delayed hypersensitivity reactions to the carrier were first detected in the absence of anaphylactic reactions which appeared later. The capabilities of macrophage-ingested antigen to induce delayed hypersensitivity reactions, but not anaphylaxis, decreased when increasing the incubation time of macrophages with antigen. The antigenic competition between hapten
and carrier was confirmed to be a transient phenomenon occurring in the macrophage.

L4 ANSWER 29 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82183231 EMBASE
DOCUMENT NUMBER: 1982183231
TITLE: Antigen presentation by peritoneal macrophages from young adult and old mice.
AUTHOR: Perkins E.H.; Massucci J.M.; Glover P.L.
CORPORATE SOURCE: Biol. Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830, United States
SOURCE: Cellular Immunology, (1982) 70/1 (1-10).
CODEN: CLIMB8
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
020 Gerontology and Geriatrics
025 Hematology
LANGUAGE: English
AB Macrophages perform vital inductive and regulatory functions in immune processes and host defence mechanisms. However, macrophage function during senescence has not been extensively studied. Although antibody response is dramatically reduced in old animals, antigen presentation has never been directly assessed. Therefore, the antigen-presenting capabilities of purified peritoneal macrophages from young adult and old mice were studied by quantitatively measuring their ability to induce antigen specific proliferation of lymph node T lymphocytes. Increasing numbers (102 to 105) of macrophages from nonimmunized young adult (3 to 6 months) or aged (27 to 36 months) animals
were cultured in the presence of antigen with a constant number (2 x 105) of column-separated popliteal lymph node cells from young adult mice. The latter had been immunized with the dinitrophenyl conjugate of bovine .gamma.-globulin in complete Freund's adjuvant by footpad injection. Macrophages from old animals were equal to macrophages from young adult animals in stimulating T-lymphocyte proliferation, and the kinetics of incorporation was identical with increasing numbers of macrophages from either young or old animals. However, greater numbers of resident or induced peritoneal macrophages were always harvested from old animals. Differences in macrophage activity as assessed by different functional parameters may be reconciled by implicating subpopulations of macrophages that perform separate functions, e.g., Ia-positive antigen presenter and Ia-negative scavenger macrophages.

L4 ANSWER 30 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 80173270 EMBASE
DOCUMENT NUMBER: 1980173270
TITLE: Ability of an anti-T-cell serum to dissociate two features of cellular hypersensitivity in the guinea-pig.
AUTHOR: Godfrey H.P.; Koch C.
CORPORATE SOURCE: Dept. Pathol., Hlth Sci. Cent., State Univ. New York, Stony Brook, N.Y. 11794, United States
SOURCE: Immunology, (1980) 40/2 (247-253).
CODEN: IMMUAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
013 Dermatology and Venereology
LANGUAGE: English
AB Guinea-pigs immunized with reactive 2,4-dinitrophenyl (DNP) sensitizer in Freund's complete adjuvant develop delayed-onset reactivities to the reactive DNP sensitizer and to DNP protein conjugates as well as to PPD. The authors have studied the role of various lymph node lymphocyte populations from these animals in producing the lymphokine macrophage agglutination factor (MAggF) and effecting antigen induced blast transformation. The production of MAggF, when elicited by reactive sensitizer or PPD, was readily inhibited by low doses of a particular cytotoxic rabbit anti-T (thymus-dependent)-lymphocyte serum and complement, while the production of MAggF when elicited by DNP protein conjugate was inhibited only by higher doses of anti-T-cell serum. These results in vitro paralleled earlier observations in vivo. In contrast, PPD induced blast transformation was only inhibited by high doses of anti-T-cell serum and not by low doses. Chromatography of sensitized lymph node cells over anti-Ig-containing columns (to remove B cells) affected neither MAggF production nor blast transformation. The authors' data suggest that these in vitro responses are mediated by 2 different subpopulations of T cells.

L4 ANSWER 31 OF 34 MEDLINE
ACCESSION NUMBER: 79129651 MEDLINE
DOCUMENT NUMBER: 79129651
TITLE: Attempts to modulate the immune response to a hapten-carrier complex with various hapten-containing compounds.
AUTHOR: Neveu P J
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1979) 58 (3) 331-6.
Journal code: GP9. ISSN: 0020-5915.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197907
AB The immune response to a hapten-carrier conjugate appears to be a complex phenomenon where reactions of the T-cell population are not restricted to the carrier and where the reactions of the B-cell population are not limited to the hapten determinant of the antigen molecule. To get a better understanding of the different cell interactions during the immune response to a hapten-carrier complex, the effects of immunogenic or tolerogenic injections of various hapten-containing compounds on the responses induced by immunization with the same hapten coupled to protein carriers were studied. The results indicate that T cells involved in delayed hypersensitivity and T cells involved in contact dermatitis could belong to distinct subclasses and confirm that hapten and carrier moieties of the antigen molecule could compete, probably at the macrophage level, for both delayed hypersensitivity to the carrier and antibody synthesis to the hapten.

L4 ANSWER 32 OF 34 CANCERLIT
ACCESSION NUMBER: 79801273 CANCERLIT
DOCUMENT NUMBER: 79801273
TITLE: MODULATION OF ANTIBODY SYNTHESIS BY AN ANTI-TUMOUR ALGA.
AUTHOR: Neveu P J; Morin O; Miegeville M; Le Mevel B P; Vermeil C
CORPORATE SOURCE: Formation de Recherche Associee No. 13, INSERM, F-44035 Nantes, France.
SOURCE: Experientia, (1978). Vol. 34, No. 12, pp. 1644-1645. ISSN: 0014-4754.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: CATH
LANGUAGE: English
ENTRY MONTH: 197903
AB The effects of a unicellular alga, Chlorella pyrenoidosa (strain 211/8b), on responses to a hapten-carrier conjugate, were assessed in Hartley guinea pigs immunized with dinitrophenylated bovine gamma globulin

(DNP48BGG: 4 mg, iv, day 0). The alga (5 x 10(6)) was administered iv on days-30,-15, and 0 or at doses of 5 x 10(8) on days -9, 0 and +3. Other animals were injected sc into the hind footpads with doses of 4 x 10(8), 4 x 10(7), or 4 x 10(6) alga emulsified in 0.1 ml Freund's incomplete adjuvant (FIA) with 50 ug of DNP48BGG; these animals were skin tested at days 8 and 12 after immunization for different types of hypersensitivities. Delayed hypersensitivity (DH) was measured by injection of 0.1, 1, and 10 ug of BGG in 0.1 ml saline 24 hr before sacrifice. Arthus and anaphylaxis types of hypersensitivities were tested. When injected iv, whatever the doses used or the interval of time chosen between treatment and iv immunization, C. pyrenoidosa had no effect on any of the responses induced by immunization with the hapten-carrier complex. Guinea-pigs exhibited a strong but transient dose-dependent inflammation of the foot pads after sc injection. Animals treated with higher doses showed depressed anaphylactic reactions on day 8 and day 12. On day 12, animals injected with 4 x 10(6) and 4 x 10(7) alga exhibited anaphylactic reactions to the carrier of approx 12.6 mm and 12.4 mm (Evans blue extrasation diameters), respectively, while controls and animals injected with 4 x 10(8) alga exhibited no reaction to the carrier. On day 16, anaphylactic reactions exhibited in treated animals equaled those of controls. Arthus reactions and hemagglutinating **antibody** kinetics in all groups were similar to those of anaphylactic reactions. No DH reactions were elicited by C. pyrenoidosa. Algal modulation of the immune response at the **macrophage** level is suspected by virtue of the initiation of antigenic competition between hapten and carrier. (12 Refs)

L4 ANSWER 33 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 77202893 EMBASE
DOCUMENT NUMBER: 1977202893
TITLE: Hapten specific responses to contact sensitizers. Use of fluorodinitrobenzene to elicit migration inhibition and **macrophage** agglutination factors from lymph node cells of contact sensitive guinea pigs.
AUTHOR: Godfrey H.P.
CORPORATE SOURCE: Inst. Exp. Immunol., Univ. Copenhagen
SOURCE: Immunological Communications, (1976) 30/5 (685-694).
CODEN: IMLCAV
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology
030 Pharmacology
025 Hematology
LANGUAGE: English
AB Hapten specific sensitivity of guinea pigs sensitized to dinitrophenyl (DNP) contactants and to DNP protein conjugates was investigated by skin test and by antigen induced elaboration of migration inhibition (MIF) and **macrophage** agglutination factors (MAF) from lymph node cells. The delayed contact reaction was highly specific for low doses of contactant and markedly less so for conjugates; lymph node cells elaborated both lymphokines in response to brief exposures to dinitrofluorobenzene (DNFB) or prolonged exposures to DNP conjugates. Elicitation of MAF by DNFB or DNP **conjugate** was inhibited in the presence of DNP glycine; the activity of MAF induced by DNP **conjugate** (but not that induced by DNFB) was inhibited in the presence of DNP glycine as well. These results suggest that contact sensitivity to DNP conjugates reflect two different types of hapten specific cellular sensitivity mediated by populations of cells with different antigen receptors and possibly, functionally different lymphokines.

L4 ANSWER 34 OF 34 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76006842 EMBASE
DOCUMENT NUMBER: 1976006842
TITLE: Tolerance induction with bovine .gamma. globulin in mouse radiation chimaeras depends on macrophages.
AUTHOR: Lukic M.L.; Leskowitz S.
CORPORATE SOURCE: Immunol. Res. Cent., Univ. Belgrade, Yugoslavia
SOURCE: Nature, (1974) 252/5484 (605-607).
CODEN: NATUAS
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English

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E6 3 ANAND O/AU
E7 9 ANAND O N/AU
E8 6 ANAND O P/AU
E9 1 ANAND OM P/AU
E10 285 ANAND P/AU
E11 1 ANAND P E V/AU
E12 3 ANAND P H MUSTAFA/AU

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L5 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1993:168824 BIOSIS
DOCUMENT NUMBER: PREV199395089874
TITLE: Probing the combining site of an anti-carbohydrate antibody by saturation-mutagenesis: Role of the heavy-chain CDR3 residues.
AUTHOR(S): Brummell, David A.; Sharma, Vidhya P.; **Anand, Naveen N.**; Bilous, Doris; Dubuc, Ginette; Michniewicz, Joseph; MacKenzie, C. Roger; Sadowska, Joanna; Sigurskjold, Bent W.; et al.
CORPORATE SOURCE: Inq.: Saran A. Narang, Institute Biological Sciences, National Research Council Canada, Ottawa, Ontario K1A 0R6 Canada
SOURCE: Biochemistry, (1993) Vol. 32, No. 4, pp. 1180-1187.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The carbohydrate-binding site in Fab fragments of an antibody specific for Salmonella serogroup B O-polysaccharide has been probed by site-directed mutagenesis using an Escherichia coli expression system. Of the six hypervariable loops, the CDR3 of the heavy chain was selected for exhaustive study because of its significant contribution to binding-site topography. A total of 90 mutants were produced and screened by an affinity electrophoresis/Western blotting method. Those of particular interest were further characterized by enzyme immunoassay, and on this basis seven of the mutant Fabs were selected for thermodynamic characterization by titration microcalorimetry. With regard to residues that hydrogen bond to ligand through backbone interactions, Gly-102H could not be substituted, while several side chains could be introduced at Gly-100H and Tyr-103H with relatively little effect on antigen binding. There was, however, a preference for nonpolar side chains at position 103H. Substitution of His-101H with carboxylate and amide side chains gave mutants with binding affinities approaching that of the wild type; complete side-chain removal by mutation to Gly was tolerated with a 10-fold reduction in binding constant. Analysis of binding by titration microcalorimetry revealed some dramatic thermodynamic changes hidden by the similarity of the binding constants. Similar effects were observed with residue changes in an Arg-Asp salt-bridge at the base of the loop. These results indicate that alterations to higher affinity anti-carbohydrate antibodies are characterized by an enthalpy-entropy compensation factor which allows for fundamental changes in the nature of the binding interactions but impedes engineering for increases in affinity.

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E5 1 ANAND N PREM/AU
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E7 1 ANAND NAVIN/AU
E8 5 ANAND NITYA/AU
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E10 9 ANAND O N/AU
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E12 1 ANAND OM P/AU

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L6 36 "ANAND N N"/AU

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L7 13 DUP REM L6 (23 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 98-110232 [10] WPIDS
DOC. NO. CPI: C98-036199
TITLE: Nucleic acid encoding mycobacterial protein involved in cell binding and entry - used for diagnosis of Mycobacterium infection and in vaccines for humans or animals.
DERWENT CLASS: B04 C06 C07 D16
INVENTOR(S): **ANAND, N N**; KLEIN, M H
PATENT ASSIGNEE(S): (CONN-N) CONNAUGHT LAB LTD
COUNTRY COUNT: 77
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9801559 | A1 | 980115 | (9810)* | EN | 107 |

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU ZW
AU 9733318 A 980202 (9826)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9801559 | A1 | WO 97-CA484 | 970709 |
| AU 9733318 | A | AU 97-33318 | 970709 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 9733318 | A Based on | WO 9801559 |

PRIORITY APPLN. INFO: US 96-677970 960710
AB WO 9801559 A UPAB: 980323
Isolated nucleic acid (I) encoding a mycobacterial protein (II) which is associated with cell binding and entry and has a molecular weight of about 45-60 kDa, and its fragments, are new.
Also claimed are:
(1) vectors containing (I);
(2) cells transformed with this vector;
(3) (II) and its fragments, including recombinant protein produced by the cells of (3), and
(4) 9 specified oligonucleotide primers.

USE - (I) is used in hybridisation tests to detect nucleic acid encoding (II) in a sample (specifically for diagnosis of Mycobacterium tuberculosis infection), while its fragments are used in polymerase chain reaction (PCR) to detect Mycobacterium in tissues and body fluids, also for isolating related genes.

Cells of (2) are used to make recombinant (II). (I) and (recombinant) (II), or their active fragments, are used in immunogenic compositions to generate an immune response, i.e. to protect humans and animals (specifically cattle) against mycobacterial infections.

Vaccines containing (II) are administered by subcutaneous, intradermal or intramuscular injection, or orally or nasally to mucosal surfaces. (I) may be delivered directly or in usual vectors, e.g. Salmonella or viruses.

Dwg.12/14

L7 ANSWER 2 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 97-077271 [07] WPIDS
DOC. NO. NON-CPI: N97-064170
DOC. NO. CPI: C97-024793
TITLE: Recombinant conjugate antibody mol., modified for delivering an antigen - elicits enhanced immune response without the use of adjuvant to generate antibodies which are useful in vaccines or immuno diagnosis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): **ANAND, N N**; BARBER, B H; CATERINI, J E; CATES, G C; KLEIN, M H
PATENT ASSIGNEE(S): (CONN-N) CONNAUGHT LAB LTD
COUNTRY COUNT: 71
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9640941 | A1 | 961219 | (9707)* | EN | 64 |

RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9661178 A 961230 (9716)
EP 833929 A1 980408 (9818) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9640941 | A1 | WO 96-CA400 | 960607 |
| AU 9661178 | A | AU 96-61178 | 960607 |
| EP 833929 | A1 | EP 96-918544 | 960607 |
| | | WO 96-CA400 | 960607 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 9661178 | A Based on | WO 9640941 |
| EP 833929 | A1 Based on | WO 9640941 |

PRIORITY APPLN. INFO: US 95-483576 950607
AB WO 9640941 A UPAB: 970212
Novel recombinant conjugate antibody mol. (I), comprises a monoclonal antibody (MAb) specific for a surface structure of antigen (ag.) presenting cells, genetically modified to contain at least one ag. exclusively at one or more preselected sites on the MAb; (I) is capable of delivering the ag. to the ag. presenting cells of a host and capable of eliciting an immune response to the ag. in the host. Also claimed are: (1) nucleic acid mol. (II), comprising: (a) a first nucleotide sequence encoding a chain of a MAb specific for a surface structure of ag. presenting cells, selected from the heavy or light chain of the MAb; (b) a second nucleotide sequence encoding at least 1 ag.; and (c) a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein, comprising the MAb chain and the at least 1 ag.; and (2) a vector comprising the nucleic acid mol.

USE - The recombinant conjugate antibody mol. (I), or the nucleic acid (II) encoding it, can be used in an immunogenic compsn. (claimed); the vaccines are administered in vivo to confer protection against a disease caused by the pathogen which produces the particular ag. In addition, the antibodies which are generated in response to immunisation with (I) or (II) can be isolated to provide antibodies specific for the particular antigen. These generated antibodies (pref. monoclonal) are useful diagnostically for immunodetection of the antigen (kits provided).

ADVANTAGE - The recombinant conjugate Ab mol. has been genetically modified to contain an ag. moiety for delivery of the ag. moiety to ag. presenting cells of immune systems, to elicit an enhanced immune response without the use of an adjuvant.

Dwg.5C/10

L7 ANSWER 3 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 93144322 MEDLINE
DOCUMENT NUMBER: 93144322
TITLE: Probing the combining site of an anti-carbohydrate antibody by saturation-mutagenesis: role of the heavy-chain CDR3 residues.
AUTHOR: Brummell D A; Sharma V P; **Anand N N**; Bilous D; Dubuc G; Michniewicz J; MacKenzie C R; Sadowska J; Sigurskjold B W; Sinnott B; et al
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ontario..
SOURCE: BIOCHEMISTRY, (1993 Feb 2) 32 (4) 1180-7.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
AB The carbohydrate-binding site in Fab fragments of an antibody specific for Salmonella serogroup B O-polysaccharide has been probed by site-directed mutagenesis using an Escherichia coli expression system. Of the six hypervariable loops, the CDR3 of the heavy chain was selected for exhaustive study because of its significant contribution to binding-site topography. A total of 90 mutants were produced and screened by an affinity electrophoresis/Western blotting method. Those of particular interest were further characterized by enzyme immunoassay, and on this basis seven of the mutant Fabs were selected for thermodynamic characterization by titration microcalorimetry. With regard to residues that hydrogen bond to ligand through backbone interactions, Gly102H could not be substituted, while several side chains could be introduced at Gly100H and Tyr103H with relatively little effect on antigen binding. There was, however, a preference for nonpolar side chains at position 103H. Substitution of His101H with carboxylate and amide side chains gave mutants with binding affinities approaching that of the wild type; complete side-chain removal by mutation to Gly was tolerated with a 10-fold reduction in binding constant. Analysis of binding by titration microcalorimetry revealed some dramatic thermodynamic changes hidden by the similarity of the binding constants. Similar effects were observed with residue changes in an Arg-Asp salt-bridge at the base of the loop. These results indicate that alterations to higher affinity anti-carbohydrate antibodies are characterized by an enthalpy-entropy compensation factor which allows for fundamental changes in the nature of the binding interactions but impedes engineering for increases in affinity.

L7 ANSWER 4 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1992:480900 BIOSIS
DOCUMENT NUMBER: BA94:112275
TITLE: STEROIDS AND RELATED STUDIES PART 87 3-2 DIALKYLAMINOETHOXY-17-BETA-DIMETHYLAMINO-1 3 5-10-ESTRATRIENE DIMETHIODIDES.
AUTHOR(S): KUMAR M; **ANAND N N**; BHARDWAJ T R; SINGH H; PATNAIK G K; DHAWAN B N
CORPORATE SOURCE: DEP. PHARMACEUTICAL SCI., PANJAB UNIVERSITY, CHANDIGARH 160 014.
SOURCE: INDIAN J CHEM SECT B ORG CHEM INCL MED CHEM, (1992) 31 (6), 322-325.
CODEN: IJSBDB. ISSN: 0376-4699.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The 3-(2-dialkylaminoethoxy)-17.beta.-dimethylamino-1,3,5,(10)-estratriene dimethiodides 2, 3 and 4 have been designed as potential neuromuscular blocking agents. They are active but none proved to be better than the prototype chandonium iodide (1). During synthesis of these quaternary compounds different steroidal amines are obtained. The hydrochlorides of the amines show no significant antiarrhythmic activity.

L7 ANSWER 5 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92042098 MEDLINE
DOCUMENT NUMBER: 92042098
TITLE: Bacterial expression and secretion of various single-chain Fv genes encoding proteins specific for a Salmonella serotype B O-antigen.
AUTHOR: **Anand N N**; Mandal S; MacKenzie C R; Sadowska J; Sigurskjold B; Young N M; Bundle D R; Narang S A
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ontario..
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Nov 15) 266 (32) 21874-9.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199202
AB Active single-chain Fv molecules encoded by synthetic genes have been expressed and secreted to the periplasm of Escherichia coli using the ompA secretory signal. Four different constructs were developed to investigate the effects of peptide linker design and VL-VH orientation on expression, secretion, and binding to a Salmonella O-polysaccharide antigen. Peptide linker sequences derived from the elbow regions of the Fab molecule were used alone or in combination with the flexible (GGGGS)2 sequence. VL and VH domain order in the single chain molecules had a profound effect on the level of secretion but hardly influenced total expression levels, which were approximately 50 mg/liter, chiefly in the form of inclusion bodies. With VL in the NH2-terminal position, the amount of secreted product obtained was 2.4 mg/liter, but when VH occupied this position the yield was less than 5% of this value. Enzyme immunoassays of the four products showed domain order and linker sequence affected antigen binding by less than an order of magnitude. Attempts to express active Fv from dicistronic DNA were unsuccessful, but active Fv was obtained from single-chain Fv by enzymic cleavage at a site in the elbow linker peptide. The thermodynamic binding parameters of intact and cleaved single-chain Fvs determined by titration microcalorimetry were similar to those of bacterially produced Fab and mouse IgG.

L7 ANSWER 6 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91276259 MEDLINE
DOCUMENT NUMBER: 91276259
TITLE: Synthesis and expression in Escherichia coli of cistronic DNA encoding an antibody fragment specific for a Salmonella serotype B O-antigen.
AUTHOR: **Anand N N**; Dubuc G; Phipps J; MacKenzie C R; Sadowska J; Young N M; Bundle D R; Narang S A
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ontario..
SOURCE: GENE, (1991 Apr) 100 39-44.
Journal code: FOP. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M74490; GENBANK-M74306; GENBANK-M62974; GENBANK-M62975; GENBANK-S70115; GENBANK-S70117; GENBANK-S70121; GENBANK-S70125; GENBANK-S70128; GENBANK-S70130
ENTRY MONTH: 199110
AB A 1460-bp DNA encoding the two chains of the antigen-binding fragment (Fab) portion of a monoclonal antibody have been chemically synthesized and expressed in Escherichia coli. The antibody, Se155-4, is specific for

a Salmonella serogroup B O-antigen and its crystal structure is under investigation. The genes were synthesized according to a strategy that allows for easy manipulation in genetic engineering studies of the Fab-binding site. Each gene is preceded by the ompA secretory signal and a ribosome-binding site, and has been expressed from the two-cistron DNA under the control of the lac promoter. Active Fab of 50 kDa with an inter-chain disulfide bond has been isolated from the periplasm of E. coli in a one-step affinity purification in high yield (2 micrograms/ml of cells). The bacterially produced Fab is as active as purified mouse Fab in antigen-binding and competitive immunoassays. This is the first example of a completely synthetic Fab gene and provides an ideal system to probe the nature of antigen binding by anti-carbohydrate antibodies.

L7 ANSWER 7 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 90319068 MEDLINE
DOCUMENT NUMBER: 90319068
TITLE: Synthesis and expression in Escherichia coli of DNA encoding the murine lambda 1 chain of a monoclonal antibody specific for Salmonella serotype B O-antigen.
AUTHOR: **Anand N N**; Dubuc G; Mandal S; Phipps J; Gidney M A; Sinnott B; Young N M; MacKenzie C R; Bundle D R; Narang S A
CORPORATE SOURCE: Division of Biological Sciences, National Research Council of Canada, Ottawa, Ontario..
SOURCE: PROTEIN ENGINEERING, (1990 May) 3 (6) 541-6.
Journal code: PR1. ISSN: 0269-2139.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
AB A 658 bp DNA sequence corresponding to the murine lambda 1 chain of a monoclonal antibody, Se155-4, specific for the Salmonella serotype B O-antigen, was designed using Escherichia coli preferred codons and chemically synthesized by ligation of synthetic fragments into a linearized plasmid followed by transformation into E. coli. A synthetic signal peptide (ompA) was fused to express the L chain as a free polypeptide into the periplasm of E. coli cells. After isolation and purification, heterologous recombination of the E. coli L chain with mouse H chain gave an active antigen-binding protein. The activity was 15-20% when compared to protein created by an equivalent association of isolated natural mouse L and H chains as measured by a direct EIA assay. In inhibition experiments with the polysaccharide antigen, the two proteins showed identical titration curves and 50% inhibition points, indicating comparable KA values.

L7 ANSWER 8 OF 13 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 88251428 MEDLINE
DOCUMENT NUMBER: 88251428
TITLE: Mutation of active site residues in synthetic T4-lysozyme gene and their effect on lytic activity.
AUTHOR: **Anand N N**; Stephen E R; Narang S A
CORPORATE SOURCE: Division of Biological Sciences, National Research Council of Canada, Ottawa..
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1988 Jun 16) 153 (2) 862-8.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-M20840
ENTRY MONTH: 198809
AB The active site amino acids (Glu11 and Asp20) in T4-lysozyme have been mutated to their isosteric residues Gln or Asn and/or acidic residues such as Glu----Asp or Asp----Glu by the oligonucleotide-replacement method. Out of eight mutants so generated the mutant T4-lysozyme obtained from pTLY.Asp11 retains maximum amount of activity (approximately 16%), pTLY.Asn20 the least (0.9%) whereas pTLY.Gln11 lost completely. A systematic study of the active and inactive mutants thus generated supports the important role of Glu11 and Asp20 in T4-lysozyme activity as predicted in earlier studies.

L7 ANSWER 9 OF 13 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 87280083 MEDLINE
DOCUMENT NUMBER: 87280083
TITLE: The structure of guanosine-thymidine mismatches in B-DNA at 2.5-A resolution.
AUTHOR: Hunter W N; Brown T; Kneale G; **Anand N N**; Rabinovich D; Kennard O
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1987 Jul 25) 262 (21) 9962-70.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198711
AB The structure of the deoxyoligomer d(C-G-C-G-A-A-T-T-T-G-C-G) was determined at 2.5-A resolution by single crystal x-ray diffraction techniques. The final R factor is 18% with the location of 71 water molecules. The oligomer crystallizes in a B-DNA-type conformation, with two strands interacting to form a dodecamer duplex. The double helix consists of four A X T and six G X C Watson-Crick base pairs and two G X T mismatches. The G X T pairs adopt a "wobble" structure with the thymine projecting into the major groove and the guanine into the minor groove. The mispairs are accommodated in the normal double helix by small adjustments in the conformation of the sugar phosphate backbone. A comparison with the isomorphous parent compound containing only Watson-Crick base pairs shows that any changes in the structure induced by the presence of G X T mispairs are highly localized. The global conformation of the duplex is conserved. The G X T mismatch has already been studied by x-ray techniques in A and Z helices where similar results were found. The geometry of the mispair is essentially identical in all structures so far examined, irrespective of the DNA conformation. The hydration is also similar with solvent molecules bridging the functional groups of the bases via hydrogen bonds. Hydration may be an important factor in stabilizing G X T mismatches. A characteristic of Watson-Crick paired A X T and G X C bases is the pseudo 2-fold symmetry axis in the plane of the base pairs. The G X T wobble base pair is pronouncedly asymmetric. This asymmetry, coupled with the disposition of functional groups in the major and minor grooves, provides a number of features which may contribute to the recognition of the mismatch by repair enzymes.

L7 ANSWER 10 OF 13 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 88040447 MEDLINE
DOCUMENT NUMBER: 88040447
TITLE: The stability of oligodeoxyribonucleotide duplexes containing degenerate bases.
AUTHOR: **Anand N N**; Brown D M; Salisbury S A
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Cambridge, UK..
SOURCE: NUCLEIC ACIDS RESEARCH, (1987 Oct 26) 15 (20) 8167-76.
Journal code: O8L. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198802
AB Oligodeoxyribonucleotides containing N4-methoxycytosine (mo4C), N4-methoxy-5-methylcytosine (mo4m5C) and other base-analogues were synthesised and used to compare the stabilities of duplexes containing mo4C.A and mo4C.G base pairs with those containing normal and mismatch pairs. The Tm values and other thermodynamic parameters are recorded. The otherwise identical duplexes containing a mo4C.A and a mo4C.G base pair have closely similar stabilities to each other and to the corresponding duplexes containing normal base pairs, considerably greater than the stabilities of those containing mismatch pairs. Corresponding observations are recorded in dot-blot experiments using M13 cloned DNA carrying an insert complementary to the oligonucleotides; approximate Td values are given.

L7 ANSWER 11 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 9
ACCESSION NUMBER: 1987:414760 BIOSIS
DOCUMENT NUMBER: BR33:84438
TITLE: BASE ANALOGUE INTERACTIONS IN DNA DUPLEXES.
AUTHOR(S): BROWN D M; **ANAND N N**; SALISBURY S A
CORPORATE SOURCE: LAB. MOL. BIOL., HILLS RD., CAMBRIDGE, ENGL.
SOURCE: 7TH INTERNATIONAL ROUND TABLE ON NUCLEOSIDES, NUCLEOTIDES AND THEIR BIOLOGICAL APPLICATIONS, KONSTANZ, WEST GERMANY, SEPTEMBER 30-OCTOBER 3, 1986. NUCLEOSIDES NUCLEOTIDES, (1987) 6 (1-2), 317-320.
CODEN: NUNUD5. ISSN: 0732-8311.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L7 ANSWER 12 OF 13 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 86175074 MEDLINE
DOCUMENT NUMBER: 86175074
TITLE: Structure of an adenine-cytosine base pair in DNA and its implications for mismatch repair.
AUTHOR: Hunter W N; Brown T; **Anand N N**; Kennard O
SOURCE: NATURE, (1986 Apr 10-16) 320 (6062) 552-5.
Journal code: NSC. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198607
AB Mutational pathways rely on introducing changes in the DNA double helix. This may be achieved by the incorporation of a noncomplementary base on replication or during genetic recombination, leading to substitution mutation. In vivo studies have shown that most combinations of base-pair mismatches can be accommodated in the DNA double helix, albeit with varying efficiencies. Fidelity of replication requires the recognition and excision of mismatched bases by proofreading enzymes and post-replicative mismatch repair systems. Rates of excision vary with the type of mismatch and there is some evidence that these are influenced by the nature of the neighbouring sequences. However, there is little experimental information about the molecular structure of mismatches and their effect on the DNA double helix. We have recently determined the crystal structures of several DNA fragments with guanine X thymine and adenine X guanine mismatches in a full turn of a B-DNA helix and now report the nature of the base pairing between adenine and cytosine in an isomorphous fragment. The base pair found in the present study is novel and we believe has not previously been demonstrated. Our results suggest that the enzymatic recognition of mismatches is likely to occur at the level of the base pairs and that the efficiency of repair can be correlated with structural features.

L7 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 85:403969 SCISEARCH
THE GENUINE ARTICLE: AMG08
TITLE: MISMATCHES IN DNA - MEASUREMENT OF REDUCED DUPLEX STABILITY USING H-1-NMR SPECTROSCOPY
AUTHOR: SALISBURY S A (Reprint); **ANAND N N**
CORPORATE SOURCE: UNIV CAMBRIDGE, CHEM LAB, LENSFIELD RD, CAMBRIDGE CB2 1EW, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-CHEMICAL COMMUNICATIONS, (1985) No. 14, pp. 985-986.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 8

=> e barber brian h/au

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|---|---|---|
| E1 | 3 | BARBER BRENT A/AU |
| E2 | 1 | BARBER BRENT J/AU |
| E3 | 13 --> | BARBER BRIAN H/AU |
| E4 | 1 | BARBER BRIAN L/AU |
| E5 | 17 | BARBER BRUCE J/AU |

09/007,093

E6 391 BARBER C/AU
E7 6 BARBER C A/AU
E8 6 BARBER C B/AU
E9 1 BARBER C B D/AU
E10 15 BARBER C C/AU
E11 12 BARBER C D/AU
E12 85 BARBER C E/AU

=> s e3

L8 13 "BARBER BRIAN H"/AU

=> d l8 1-13

L8 ANSWER 1 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:485422 BIOSIS
DN PREV199800485422
TI Predominant role for directly transfected dendritic cells in antigen presentation to CD8+ T cells after gene gun immunization.
[redacted] Porgador, Angel; Irvine, Kari R.; Iwasaki, Akiko; **Barber, Brian H.**
[redacted] Restifo, Nicholas P.; Germain, Ronald N. (1)
CS (1) Lab Immunol., Build. 10, 11N311, 10 Center Dr. MSC-1892, Bethesda, MD
20892-1892 USA
SO Journal of Experimental Medicine, (Sept. 21, 1998) Vol. 188, No. 6, pp. 1075-1082.
ISSN: 0022-1007.
DT Article
LA English

L8 ANSWER 2 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:167578 BIOSIS
DN PREV199800167578
TI Mother-child class I HLA concordance increases perinatal human immunodeficiency virus type 1 transmission.
AU MacDonald, Kelly S. (1); Embree, Joanne; Njenga, Simon; Nagelkerke, Nico
J. D.; Ngatia, Irene; Mohammed, Zeena; **Barber, Brian H.**; Ndinya-Achola, Jeckoniah; Bwayo, Job; Plummer, Francis A.
CS (1) Mount Sinai Hosp., 1484-600 University Ave., Toronto, ON M5G 1X5 Canada
SO Journal of Infectious Diseases, (March, 1998) Vol. 177, No. 3, pp. 551-556.
ISSN: 0022-1899.
DT Article
LA English

[redacted] ANSWER 3 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
1998:138404 BIOSIS
PREV199800138404
TI Induction by DNA immunization of a protective antitumor cytotoxic T lymphocyte response against a minimal-epitope-expressing tumor.
AU Iwasaki, Akiko; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Med. Sci. Building, Univ. Toronto, Toronto, ON M5S 1A8 Canada
SO Cancer Immunology Immunotherapy, (Jan., 1998) Vol. 45, No. 5, pp. 273-279.
ISSN: 0340-7004.
DT Article
LA English

L8 ANSWER 4 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:121638 BIOSIS
DN PREV199800121638
TI Naturally occurring IgG anti-HLA alloantibody does not correlate with HIV type 1 resistance in Nairobi prostitutes.
AU Luscher, Mark A.; Choy, Gregory; Njagi, Ephantas; Bwayo, Job J.; Anzala, Aggrey O.; Ndinya-Achola, Jackoniah O.; Ball, T. Blake; Wade, Judy A.; Plummer, Francis A.; **Barber, Brian H.**; Macdonald, Kelly S. (1)
CS (1) Dep. Microbiol., Mt. Sinai Hosp., 1484-600 University Ave., Toronto, ON M5G 1X5 Canada
SO AIDS Research and Human Retroviruses, (Jan. 20, 1998) Vol. 14, No. 2, pp.
109-115.
ISSN: 0889-2229.
DT Article
LA English

L8 ANSWER 5 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:121637 BIOSIS
DN PREV199800121637
TI Anti-HLA alloantibody is found in children but does not correlate with a lack of HIV type 1 transmission from infected mothers.
AU Luscher, Mark A.; Choy, Gregory; Embree, Joanne E.; Nagelkerke, Nicolaas
J. D.; Bwayo, Job J.; Njenga, Simon; Plummer, Francis A.; **Barber, Brian H.**; Macdonald, Kelly S. (1)
CS (1) Dep. Microbiol., Mt. Sinai Hosp., 1484-600 University Ave., Toronto, ON M5G 1X5 Canada
SO AIDS Research and Human Retroviruses, (Jan. 20, 1998) Vol. 14, No. 2, pp.
99-107.
ISSN: 0889-2229.
DT Article
LA English

L8 ANSWER 6 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:220079 BIOSIS
DN PREV199799526583
TI Recombinant antibodies with conformationally constrained HIV type 1 epitope inserts elicit glycoprotein 160-specific antibody responses in vivo.
AU Cook, Jeremy; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Med. Sci. Build., 1 King's College Circle, Univ. Toronto, Toronto, ON M5S 1A8 Canada
SO AIDS Research and Human Retroviruses, (1997) Vol. 13, No. 6, pp. 449-460.
ISSN: 0889-2229.
DT Article
LA English

L8 ANSWER 7 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:77056 BIOSIS
DN PREV199698649191
TI Recombinant antibodies containing an engineered B-cell epitope capable of eliciting conformation-specific antibody responses.
AU Cook, Jeremy; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Med. Sci. Building, University Toronto, Toronto, ON M5S 1A8 Canada
SO Vaccine, (1995) Vol. 13, No. 18, pp. 1770-1778.
ISSN: 0264-410X.
DT Article
LA English

L8 ANSWER 8 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:35427 BIOSIS
DN PREV199598049727
TI Characteristics of heterologous beta-2-m exchange into H-2D-b at the cell surface.
AU Luscher, Mark A.; Newton, Barbara L.; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Univ. Toronto, 1 King's Coll. Circle, Toronto, ON, M5S 1A8 Canada
SO Journal of Immunology, (1994) Vol. 153, No. 11, pp. 5068-5081.
ISSN: 0022-1767.
DT Article
LA English

L8 ANSWER 9 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:526924 BIOSIS
DN PREV199396140331
TI Studies of the adjuvant-independent antibody response to immunotargeting: Target structure dependence, isotype distribution, and induction of long term memory.
AU Skea, Danna L.; **Barber, Brian H.**
CS Dep. Immunol., Med. Sci. Build., Univ. Toronto, Toronto, ON, Canada M5S 1A8
SO Journal of Immunology, (1993) Vol. 151, No. 7, pp. 3557-3568.
ISSN: 0022-1767.
DT Article
LA English

L8 ANSWER 10 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:523459 BIOSIS
DN PREV199396136866
TI High occupancy binding of antigenic peptides to purified, immunoadsorbed H-2D-b beta-2m molecules.
AU Burshytn, Deborah N.; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Medical Sci. Building, Univ. Toronto, Toronto, M5s 1A8 Canada
SO Journal of Immunology, (1993) Vol. 151, No. 6, pp. 3070-3081.
ISSN: 0022-1767.
DT Article
LA English

L8 ANSWER 11 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:523458 BIOSIS
DN PREV199396136865
TI Dynamics of peptide binding to purified antibody-bound H-2D-b and H-2D-b-beta-2m complexes.
AU Burstyn, Deborah N.; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Medical Sci. Building, Univ. Toronto, Toronto M5S 1A8 Canada
SO Journal of Immunology, (1993) Vol. 151, No. 6, pp. 3082-3093.
ISSN: 0022-1767.
DT Article
LA English

L8 ANSWER 12 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:458876 BIOSIS
DN PREV199396103776
TI Adhesion-mediated enhancement of the adjuvant activity of alum.
AU Skea, Danna L.; **Barber, Brian H. (1)**
CS (1) Dep. Immunol., Univ. Toronto, Toronto ON M5S 1A8 Canada
SO Vaccine, (1993) Vol. 11, No. 10, pp. 1018-1026.
ISSN: 0264-410X.
DT Article
LA English

L8 ANSWER 13 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:241631 BIOSIS
DN PREV199344114831
TI Assembly and thermostability of purified class I complexes.
AU Burshtyn, Deborah N.; **Barber, Brian H.**
CS Dep. Immunol., Univ. Toronto, Toronto, ON M5S 1A8 Canada
SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART C,
pp. 54.
Meeting Info.: Keystone Symposium on Emerging Principles for Vaccine Development: Antigen Processing and Presentations Taos, New Mexico, USA
February 8-14, 1993
ISSN: 0733-1959.
DT Conference
LA English

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E1 8 CATES G W/AU
E2 2 CATES GEORGE/AU
E3 1 --> CATES GEORGE A/AU
E4 4 CATES GORDON D/AU
E5 9 CATES H/AU
E6 4 CATES H B/AU
E7 19 CATES H E/AU
E8 1 CATES HAL/AU
E9 17 CATES J/AU
E10 106 CATES J A/AU
E11 14 CATES J C/AU
E12 47 CATES J D/AU

=> s e2 or e3

L9 3 "CATES GEORGE"/AU OR "CATES GEORGE A"/AU

09/007,093

=> d l9 1-3

L9 ANSWER 1 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:444849 BIOSIS
DN PREV199800444849
TI Protection against respiratory syncytial virus infection by DNA immunization.
AU Li, Xiaomao (1); Sambhara, Suryaprakash; Li, Cindy Xin; Ewasyshyn, Mary;
Parrington, Mark; Caterini, Judy; James, Olive; **Cates, George**;
Du, Run-Pan; Klein, Michel
CS (1) Res. Cent., Pasteur Merieux Connaught Canada, 1755 Steeles Ave. West,
North York, ON M2R 3T4 Canada
SO Journal of Experimental Medicine, (Aug. 17, 1998) Vol. 188, No. 4, pp. 681-688.
ISSN: 0022-1007.
DT Article
LA English

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:278462 BIOSIS
DN PREV199699000818
TI Developmental expression of the collagen-binding heat-shock protein GP46 and collagen types I and IV in rat tissues.
AU Pak, Brian J.; Wigle, Dennis A.; Watson, John D.; **Cates, George A.**
; Brickenden, Anne M.; Ball, Eric H.; Pang, Stephen C. (1)
CS (1) Dep. Anat. Cell Biol., Queen's Univ., Kingston, ON K7L 3N6 Canada
SO Biochemistry and Cell Biology, (1996) Vol. 74, No. 2, pp. 179-185.
ISSN: 0829-8211.
DT Article
LA English
SL English; French

L9 ANSWER 3 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:56979 BIOSIS
DN PREV199698629114
TI Induction of HIV type 1 neutralizing and env-CD4 blocking antibodies by immunization with genetically engineered HIV type 1-like particles containing unprocessed gp160 glycoproteins.
AU Rovinski, Benjamin (1); Rodrigues, Lauren; Cao, Shi Xian; Yao, Fei-Long; McGuinness, Ursula; Sia, Charles; **Cates, George**; Zolla-Pazner, Susan; Karwowska, Sylwia; Matthews, Thomas J.; McDanal, Charlene B.; Mascola, John; Klein, Michel H.
CS (1) Dep. Mol. Virol., Connaught Centre Biotechnol. Res., 1755 Steeles Ave. West, Willowdale, ON M2R 3T4 Canada
SO AIDS Research and Human Retroviruses, (1995) Vol. 11, No. 10, pp. 1187-1195.
ISSN: 0889-2229.
DT Article
LA English

=> e barber b h/au

E1 4 BARBER B D/AU
E2 1 BARBER B E/AU
E3 252 --> BARBER B H/AU
E4 284 BARBER B J/AU
E5 5 BARBER B K/AU
E6 45 BARBER B L/AU
E7 22 BARBER B P/AU
E8 51 BARBER B R/AU
E9 1 BARBER B S/AU
E10 1 BARBER B T/AU
E11 2 BARBER B W/AU
E12 1 BARBER BARBARA/AU

=> s e3 and antibod?

3 FILES SEARCHED...
L10 102 "BARBER B H"/AU AND ANTIBOD?

=>
Connection closed by remote host

09/007,093

FILE 'USPAT' ENTERED AT 16:18:18 ON 30 MAR 1999

WELCOME TO THE
U.S. PATENT TEXT FILE

=> s (antibod? or monoclon?)(p)(conjugate or fusion protein or chimer?)(p)(apc or antigen presenting cell or kupffer cell or langerhans cell or macrophage)(p) adjuvant

34618 ANTIBOD?
16813 MONOCLON?
21900 CONJUGATE
7360 CONJUGATES
23925 CONJUGATE
(CONJUGATE OR CONJUGATES)
45374 FUSION
3056 FUSIONS
45724 FUSION
(FUSION OR FUSIONS)
70615 PROTEIN
55502 PROTEINS
84289 PROTEIN
(PROTEIN OR PROTEINS)
5505 FUSION PROTEIN
(FUSION(W)PROTEIN)
5313 CHIMER?
2172 APC
189 APCS
2235 APC
(APC OR APCS)
23364 ANTIGEN
15499 ANTIGENS
26133 ANTIGEN
(ANTIGEN OR ANTIGENS)
59088 PRESENTING
2 PRESENTINGS
59090 PRESENTING
(PRESENTING OR PRESENTINGS)
227160 CELL
184310 CELLS
270884 CELL
(CELL OR CELLS)
731 ANTIGEN PRESENTING CELL
(ANTIGEN(W)PRESENTING(W)CELL)
350 KUPFFER
227160 CELL
184310 CELLS
270884 CELL
(CELL OR CELLS)
282 KUPFFER CELL
(KUPFFER(W)CELL)
712 LANGERHANS
227160 CELL
184310 CELLS
270884 CELL
(CELL OR CELLS)
267 LANGERHANS CELL
(LANGERHANS(W)CELL)
4335 MACROPHAGE
6134 MACROPHAGES
7920 MACROPHAGE
(MACROPHAGE OR MACROPHAGES)
18356 ADJUVANT
25766 ADJUVANTS
36132 ADJUVANT
(ADJUVANT OR ADJUVANTS)
L1 6 (ANTIBOD? OR MONOCLON?)(P)(CONJUGATE OR FUSION PROTEIN OR C
HIM
ER?)(P)(APC OR ANTIGEN PRESENTING CELL OR KUPFFER CELL OR L
ANG
ERHANS CELL OR MACROPHAGE)(P) ADJUVANT

=> d l1 1-6 leg ab

US PAT NO: 5,889,144 [IMAGE AVAILABLE] L1: 1 of 6
DATE ISSUED: Mar. 30, 1999
TITLE: Fused somatotropin epitopic peptides that potentiate growth hormone activity
INVENTOR: Hector Wasunna Alila, Malvern, PA
Michael Thomas Clark, Downington, PA
Elaine Verne Jones, Wynnewood, PA
Timothy Joe Miller, Malvern, PA
Shawn Patrick O'Brien, Hatboro, PA
Ganesh Madhusudan Sathe, King of Prussia, PA
ASSIGNEE: Pfizer Inc., New York, NY (U.S. corp.)
APPL-NO: 08/846,913
DATE FILED: Apr. 30, 1997
ART-UNIT: 166
PRIM-EXMR: John Ulm
ASST-EXMR: Christine Saoud
LEGAL-REP: Peter C. Richardson, Paul H. Ginsburg, Alan L. Koller

US PAT NO: 5,889,144 [IMAGE AVAILABLE] L1: 1 of 6

ABSTRACT:
This invention relates to composite somatotropin peptides comprising somatotropin epitopic amino acid sequences, and fusion proteins thereof, useful in potentiating growth hormone activity. Also disclosed are vectors and host cells useful in the recombinant production of such molecules. Vaccines containing the composite somatotropin peptides and fusion proteins of the present invention, and methods of using the same, are disclosed.

US PAT NO: 5,747,294 [IMAGE AVAILABLE] L1: 2 of 6
DATE ISSUED: May 5, 1998
TITLE: Compositions and methods for the prevention and diagnosis of lyme disease
INVENTOR: Richard A. Flavell, Killingworth, CT
Fred S. Kantor, Orange, CT
Stephen W. Barthold, Madison, CT
Erol Fikrig, Guilford, CT
ASSIGNEE: Yale University, New Haven, CT (U.S. corp.)
APPL-NO: 08/320,161
DATE FILED: Oct. 7, 1994
ART-UNIT: 182
PRIM-EXMR: Susan A. Loring
LEGAL-REP: James F. Haley, Jr., Esq., Jane T. Gunnison, Esq.

US PAT NO: 5,747,294 [IMAGE AVAILABLE] L1: 2 of 6

ABSTRACT:
Methods and compositions for the prevention and diagnosis of Lyme disease. OspA and OspB polypeptides and serotypic variants thereof, which elicit in a treated animal the formation of an immune response which is effective to treat or protect against Lyme disease as caused by infection with B. burgdorferi. Anti-OspA and anti-OspB antibodies that are effective to treat or protect against Lyme disease as caused by infection with B. burgdorferi. A screening method for the selection of those OspA and OspB polypeptides and anti-OspA and anti-OspB antibodies that are useful for the prevention and detection of Lyme disease. Diagnostic kits including OspA and OspB polypeptides or antibodies directed against such polypeptides.

US PAT NO: 5,691,197 [IMAGE AVAILABLE] L1: 3 of 6
DATE ISSUED: Nov. 25, 1997
TITLE: Isolated DNA sequence for a novel macrophage receptor with a collagenous domain
INVENTOR: Karl Tryggvason, Fyysinkontie 8, SF-90570 Oulu, Finland
Outi Elomaa, Asemakatu 41, 90100 Oulu, Finland
Maarit Kangas, Sipolankuja 4, 90800 Oulu, Finland
APPL-NO: 08/392,367
DATE FILED: Feb. 21, 1995
ART-UNIT: 188
PRIM-EXMR: Marianne P. Allen
ASST-EXMR: Robert C. Hayes
LEGAL-REP: Fay, Sharpe, Beall, Fagan, Minnich & McKee

US PAT NO: 5,691,197 [IMAGE AVAILABLE] L1: 3 of 6

ABSTRACT:
The present invention is directed to processes for isolating and identifying the nucleotide sequence of a gene for a novel macrophage receptor with collagenous structure, termed "MARCO". The new macrophage receptor with a collagenous domain binds gram positive and negative bacteria and acetylated LDL. Moreover, the invention relates to the nucleotide sequence for MARCO identified by the process of the invention and the isolated and purified polypeptide chain encoded by such a sequence.

US PAT NO: 5,686,268 [IMAGE AVAILABLE] L1: 4 of 6
DATE ISSUED: Nov. 11, 1997
TITLE: Fused proteins
INVENTOR: Hector Wasunna Alila, Malvern, PA
Michael Thomas Clark, Downington, PA
Elaine Verne Jones, Wynnewood, PA
Timothy Joe Miller, Malvern, PA
Shawn Patrick O'Brien, Hatboro, PA
Ganesh Madhusudan Sathe, King of Prussia, PA
ASSIGNEE: Pfizer Inc., New York, NY (U.S. corp.)
APPL-NO: 08/388,267
DATE FILED: Jan. 27, 1995
ART-UNIT: 181
PRIM-EXMR: Vasu S. Jagannathan
ASST-EXMR: Christine Saoud
LEGAL-REP: Peter C. Richardson, Paul H. Ginsburg, Alan L. Koller

US PAT NO: 5,686,268 [IMAGE AVAILABLE] L1: 4 of 6

ABSTRACT:
This invention relates to composite somatotropin peptides and fusion protein thereof useful in the potentiating of growth hormone activity. Also disclosed are vector and host cells useful in the recombinant production of such molecules. Vaccines containing composite somatotropin and fusion proteins thereof and methods of using same as disclosed.

US PAT NO: 5,194,254 [IMAGE AVAILABLE] L1: 5 of 6
DATE ISSUED: Mar. 16, 1993
TITLE: Enhancement of antigen immunogenicity
INVENTOR: Brian H. Barber, Mississauga, Canada
George Carayannotis, Toronto, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 07/421,188
DATE FILED: Oct. 13, 1989
ART-UNIT: 183
PRIM-EXMR: John W. Rollins
ASST-EXMR: Abdel A. Mohamed
LEGAL-REP: Sim & McBurney

US PAT NO: 5,194,254 [IMAGE AVAILABLE] L1: 5 of 6

ABSTRACT:
A new method is described for eliciting IgG antibody response to proteins or synthetic peptides, particularly those that are weakly immunogenic, without the requirement for the use of adjuvants, thereby making it easier and safer to confer protection against pathogenic organisms. The antigen is coupled to a monoclonal antibody, specific for membrane determinants expressed on certain types of mammalian recipient cells, called antigen presenting cells. The monoclonal antibody acts as a "vector" or "delivery vehicle" for targeting foreign antigens onto such recipient cells. This targeting facilitates subsequent antigen recognition by helper T-cells, which are pivotal in helping the induction of antigen-specific IgG responses.

US PAT NO: 4,950,480 [IMAGE AVAILABLE] L1: 6 of 6
DATE ISSUED: Aug. 21, 1990
TITLE: Enhancement of antigen immunogenicity
INVENTOR: Brian H. Barber, Mississauga, Canada
George Carayannotis, Scarborough, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 07/046,095
DATE FILED: May 5, 1987
ART-UNIT: 186
PRIM-EXMR: Garnette Draper
ASST-EXMR: Abdel A. Mohamed
LEGAL-REP: Sim & McBurney

US PAT NO: 4,950,480 [IMAGE AVAILABLE] L1: 6 of 6

ABSTRACT:
A new method is described for eliciting IgG antibody response to proteins or synthetic peptides without the requirement for the use of adjuvants, thereby making it easier and safer to confer protection against pathogenic organisms. The antigen is coupled to a monoclonal antibody, specific for membrane determinants expressed on certain types of mammalian recipient cells, called antigen presenting cells. The monoclonal antibody acts as a "vector" or "delivery vehicle" for targeting foreign antigens onto such recipient cells. This targeting facilitates subsequent antigen recognition by helper T-cells, which are pivotal in helping the induction of antigen-specific IgG responses.

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US PAT NO: 5,889,144 [IMAGE AVAILABLE] L1: 1 of 6

DETDESC:

DETD(27)

The Imject Activated Supercarrier system (Pierce) was used to **conjugate** NS1-pST to the carrier protein, BSA, to enhance **antibody** production following immunization of rabbits. This approach is based on the concept that cationized BSA will carry an antigen that is covalently coupled to it, regardless of size, into the **antigen presenting cell** (**APC**) resulting in more efficient processing and presentation of that antigen and consequently yield an enhanced immune response (Muckerheide et. al, J. Immunol. 138:833-37 (1987); Apple et. al., J. Immunol. 140:3290-95 (1988)). The antigen bound BSA is then mixed with aluminum hydroxide **adjuvant** followed by injection. The enhanced response of "Supercarrier" conjugated immunogens with this **adjuvant** can give an **antibody** titer approximately equal to that seen with incomplete Freund's **adjuvant**, but without the potential danger to the animal or to the researcher.

US PAT NO: 5,747,294 [IMAGE AVAILABLE] L1: 2 of 6

DETDESC:

DETD(190)

Stimulation in animals of a humoral immune response containing high titer neutralizing **antibodies** will be facilitated by antigens containing both T cell and B cell epitopes. To identify those OspA **fusion proteins** containing T cell epitopes we infect C3H/He mice with B. burgdorferi strain N40 in complete Freund's **adjuvant**, as described supra. Ten days after priming, lymph nodes are harvested and in vitro T cell lines are generated. These T cell lines are then cloned using limiting dilution and soft agar techniques. We use these T cell clones to determine which OspA **fusion proteins** contain T cell epitopes. The T cell clones are stimulated with the OspA **fusion proteins** and syngeneic **antigen presenting cells**. Exposure of the T cell clones to **fusion proteins** that contain T cell epitopes causes the T cells to proliferate, which we measure by .sup.3 H-Thymidine incorporation. We also measure lymphokine production by the stimulated T cell clones by standard methods.

US PAT NO: 5,691,197 [IMAGE AVAILABLE] L1: 3 of 6

DETDESC:

DETD(45)

**Monoclonal antibodies**, ERTR-1 and MOMA-1, against **macrophage** antigens have previously been described (Dijkstra, C. D., Van Vliet, E., Dopp, E. A., Van der Lelij, A. A., and Kraal, G., Marginal zone **macrophages** identified by a **monoclonal antibody**: characterization of immuno- and enzyme-histochemical properties and functional capasities, Immunology 55, 23-28 (1985); Kraal, G., Ter Hart H., Meelhuizen, C., Venneker, and Claassen, E., Marginal zone **macrophages** and their role in the immune response against T-independent type 2 antigens. Modulation of the cells with specific **antibody**, Eur. J. Immunol. 19, 675-681 (1989)). For the production of polyclonal **antibodies** domains of the MARCO polypeptide were expressed as glutathione S-transferase (GST) **fusion proteins** in the pGEX-1.lambda.T vector (Pharmacia) in E. coli. DNA fragments encoding the putative extracellular domain IV and V (residues 369-518, FIG. 2) and intracellular domain I (residues 1-50, FIG. 2) of the MARCO polypeptide were generated by polymerase chain reaction (PCR) using primers containing restriction sites for cloning into the pGEX-1.lambda.T vector (Pharmacia). Sequences were confirmed by DNA-sequencing. **Fusion proteins** produced in bacteria were purified using glutathione Sepharose 4B (Pharmacia) and eluted with 5 mM glutathione. Purified MARCO polypeptides were mixed with Freund's **adjuvant** (Difco), and used for immunization of rabbits. Antisera were used after the third booster. IgGs were first purified by protein A Sepharose (Pharmacia) and then further purified by negative immunoabsorption from unspecific **antibodies** against the GST-protein and E. coli proteins using GST-E. coli total protein lysate coupled to CNBr-activated Sepharose 4B (Pharmacia).

US PAT NO: 5,686,268 [IMAGE AVAILABLE] L1: 4 of 6

DETDESC:

DETD(81)

The Imject Activated Supercarrier system (Pierce) was used to **conjugate** NS1-pST to the carrier protein, BSA, to enhance **antibody** production following immunization of rabbits. This approach is based on the concept that cationized BSA will carry an antigen that is covalently coupled to it, regardless of size, into the **antigen presenting cell** (**APC**) resulting in more efficient processing and presentation of that antigen and consequently yield an enhanced immune response (Muckerheide et al., J. Immunol. 138:833-37 (1987); Apple et al., . J. Immunol. 140:3290-95 (1988)). The antigen bound BSA is then mixed with aluminum hydroxide **adjuvant** followed by injection. The enhanced response of "Supercarrier" conjugated immunogens with this **adjuvant** can give an **antibody** titer approximately equal to that seen with incomplete Freund's **adjuvant**, but without the potential danger to the animal or to the researcher.

US PAT NO: 5,194,254 [IMAGE AVAILABLE] L1: 5 of 6

DETDESC:

DETD(30)

As may be seen from the data presented in FIG. 1, at the 5 .mu.g dose of avidin, a significant response was observed in (B6.times.C.sub.3 H)F.sub.1 mice injected with (anti-I-A.sup.k)-avidin **conjugate** (FIG. 1A, open circles) whereas the B6 mice (FIG. 1A, closed circles), which do not have the particular surface antigens for which the **antibody** was made, were not appreciably sensitized (see FIG. 1A). This result cannot be attributed to an immuno-stimulating effect of the **antibody** alone, since the mixture of 5 .mu.g of avidin with unmodified anti-I-A.sup.k MAb did not elicit a response (FIG. 1B). An equal amount of avidin coupled to the control anti-NP MAb also failed to generate an appreciable response (FIG. 1C), indicating that the positive response shown in FIG. 1A is due to more than a simple conjugation of avidin to an **antibody**. As expected 5 .mu.g of avidin injected with Freund's complete adjuvant induced a strong serological response (FIG. 1D). At the 50 .mu.g of avidin dose, free avidin in the absence of **adjuvant** failed to stimulate a response (FIG. 1B), but in the form of (bio-anti-I-A.sup.k)-avidin, the **conjugate** sensitized both (B6.times.C3H)F.sub.1 and B6 mice (FIG. 1A). Responses in the B6 mice are likely a reflection of the elevated reactivity of the avidin-MAb **conjugate** on the B6 targets and may be attributed either to cross-reactivity of the conjugated MAb or more efficient APC uptake of the MAb-avidin complex.

DETDESC:

DETD(59)

In summary of this disclosure, the present invention provides a novel method of vaccinating mammals by the conjugation of antigens, which may be in the form of synthetic epitopes or protein subunits to **monoclonal antibodies** specific for **antigen-presenting cells** of the recipient, such that these antigen-**antibody conjugates** may be used to elicit a beneficial **antibody** response without needing to use deleterious **adjuvants**. Modifications are possible within the scope of this invention.

CLAIMS:

CLMS(8)

8. A vaccine physiologically suitable for administration to a mammal to elicit an IgG **antibody** response to an antigen, which consists essentially of a **conjugate** comprising at least one normally weakly-immunogenic antigen which is a peptide or protein against which the IgG **antibody** response is to be elicited conjugated to a **monoclonal antibody** specific for surface structures of **antigen-presenting cells** of the mammal and suitable carrier therefor, whereby said **antibody** response occurs without an immunogenicity-enhancing **adjuvant**.

US PAT NO: 4,950,480 [IMAGE AVAILABLE] L1: 6 of 6

DETDESC:

DETD(23)

As may be seen from the data presented in FIG. 1, at the 5 .mu.g dose of avidin, a significant response was observed in (B6xC3H)F.sub.1 mice injected with (anti-I-A.sup.k)-avidin **conjugate** (FIG. 1A, open circles) whereas the B6 mice (FIG. 1A, closed circles), which do not have the particular surface antigens for which the **antibody** was made, were not appreciably sensitized (see FIG. 1A). This result cannot be attributed to an immuno-stimulating effect of the **antibody** alone, since the mixture of 5 .mu.g of avidin with unmodified anti-I-A.sup.k MAb did not elicit a response (FIG. 1B). An equal amount of avidin coupled to the control anti-NP MAb also failed to generate an appreciable response (FIG. 1C), indicating that the positive response shown in FIG. 1A is due to more than a simple conjugation of avidin to an **antibody**. As expected 5 .mu.g of avidin injected with Freund's complete **adjuvant** induced a strong serological response (FIG. 1D). At the 50 .mu.g of avidin dose, free avidin in the absence of **adjuvant** failed to stimulate a response (FIG. 1B), but in the form of (bio-anti-I-A.sup.k)-avidin, the **conjugate** sensitized both (B6.times.C3H)F.sub.1 and B6 mice (FIG. 1A). Responses in the B6 mice are likely a reflection of the elevated reactivity of the avidin-MAb **conjugate** on the B6 targets and may be attributed either to cross-reactivity of the conjugated MAb or more efficient **APC** uptake of the MAb-avidin complex.

CLAIMS:

CLMS(9)

9. A vaccine physiologically suitable for administration to a mammal to elicit an IgC **antibody** response to an antigen, which consists essentially of a **conjugate** comprising a normally weakly-immunogenic antigen which is a peptide or protein bonded to a **monoclonal antibody** specific for a histocompatibility antigen present on the

surface of B-cells and macrophages and a suitable carrier therefor, whereby said antibody response occurs without an immunogenicity-enhancing adjuvant.

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| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | ANAND, KRANTI V DECEASED/IN |
| E2 | USPAT | 10 | ANAND, MADHU/IN |
| E3 | USPAT | 0 | --> ANAND, NAVEEN/IN |
| E4 | USPAT | 3 | ANAND, NITYA/IN |
| E5 | USPAT | 1 | ANAND, PRAVEEN/IN |
| E6 | USPAT | 5 | ANAND, PREM K/IN |
| E7 | USPAT | 1 | ANAND, RAJ K/IN |
| E8 | USPAT | 2 | ANAND, RAJIV/IN |
| E9 | USPAT | 5 | ANAND, RAKESH/IN |
| E10 | USPAT | 1 | ANAND, RAVI/IN |
| E11 | USPAT | 1 | ANAND, RITA/IN |
| E12 | USPAT | 1 | ANAND, SATISH/IN |

e barber, brian h/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | BARBER, BRIAN C/IN |
| E2 | USPAT | 1 | BARBER, BRIAN D/IN |
| E3 | USPAT | 3 | --> BARBER, BRIAN H/IN |
| E4 | USPAT | 1 | BARBER, BRIAN MICHAEL/IN |
| E5 | USPAT | 3 | BARBER, BRUCE/IN |
| E6 | USPAT | 2 | BARBER, BRUCE A/IN |
| E7 | USPAT | 1 | BARBER, BRUCE T/IN |
| E8 | USPAT | 1 | BARBER, BRUCE WILLIAM/IN |
| E9 | USPAT | 1 | BARBER, BY LIONEL PERSONAL REPRESENTATIVE/IN |
| E10 | USPAT | 1 | BARBER, BY WILLIAM L EXECUTOR/IN |
| E11 | USPAT | 1 | BARBER, CHARLES LAUNCELOT JR/IN |
| E12 | USPAT | 1 | BARBER, CHARLES R/IN |

=> s e3

L2 3 "BARBER, BRIAN H"/IN

=> d l2 1-3 leg ab

US PAT NO: 5,730,985 [IMAGE AVAILABLE] L2: 1 of 3
DATE ISSUED: Mar. 24, 1998
TITLE: Immunogens for the production of cocaine-hydrolyzing catalytic antibodies
INVENTOR: **Brian H. Barber**, Mississauga, Canada
Neal den Hollander, Mississauga, Canada
Jiri J. Krepinsky, Newmarket, Canada
M. Younus Meah, Ann Arbor, MI
ASSIGNEE: Governing Council of the University of Toronto, Toronto, Canada (foreign corp.)
APPL-NO: 08/259,004
DATE FILED: Jun. 13, 1994
ART-UNIT: 185
PRIM-EXMR: Michael P. Woodward
LEGAL-REP: Sim & McBurney

US PAT NO: 5,730,985 [IMAGE AVAILABLE] L2: 1 of 3

ABSTRACT:
Methods are described for the rapid synthesis in satisfactory yield of methyl ecgonine phenylphosphonates as analogues of transition states for the hydrolysis of the benzoyl ester of an ecgonine derivative, namely cocaine, and their linking to carrier proteins, for the purpose of using them as immunogens. The resulting immunogens elicit the formation in experimental animals of antibodies able to promote the hydrolysis of cocaine. Both these catalytic anti-cocaine antibodies and the immunogens themselves are potentially useful for the treatment of individuals seeking to avoid the pharmacological effects of cocaine and in diagnostic applications.

US PAT NO: 5,194,254 [IMAGE AVAILABLE] L2: 2 of 3
DATE ISSUED: Mar. 16, 1993
TITLE: Enhancement of antigen immunogenicity
INVENTOR: **Brian H. Barber**, Mississauga, Canada
George Carayannotis, Toronto, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 07/421,188
DATE FILED: Oct. 13, 1989
ART-UNIT: 183
PRIM-EXMR: John W. Rollins
ASST-EXMR: Abdel A. Mohamed
LEGAL-REP: Sim & McBurney

US PAT NO: 5,194,254 [IMAGE AVAILABLE] L2: 2 of 3

ABSTRACT:
A new method is described for eliciting IgG antibody response to proteins or synthetic peptides, particularly those that are weakly immunogenic, without the requirement for the use of adjuvants, thereby making it easier and safer to confer protection against pathogenic organisms. The antigen is coupled to a monoclonal antibody, specific for membrane determinants expressed on certain types of mammalian recipient cells, called antigen presenting cells. The monoclonal antibody acts as a "vector" or "delivery vehicle" for targeting foreign antigens onto such recipient cells. This targeting facilitates subsequent antigen recognition by helper T-cells, which are pivotal in helping the induction of antigen-specific IgG responses.

US PAT NO: 4,950,480 [IMAGE AVAILABLE] L2: 3 of 3
DATE ISSUED: Aug. 21, 1990
TITLE: Enhancement of antigen immunogenicity
INVENTOR: **Brian H. Barber**, Mississauga, Canada
George Carayannotis, Scarborough, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 07/046,095
DATE FILED: May 5, 1987
ART-UNIT: 186
PRIM-EXMR: Garnette Draper
ASST-EXMR: Abdel A. Mohamed
LEGAL-REP: Sim & McBurney

US PAT NO: 4,950,480 [IMAGE AVAILABLE] L2: 3 of 3

ABSTRACT:
A new method is described for eliciting IgG antibody response to proteins or synthetic peptides without the requirement for the use of adjuvants, thereby making it easier and safer to confer protection against pathogenic organisms. The antigen is coupled to a monoclonal antibody, specific for membrane determinants expressed on certain types of mammalian recipient cells, called antigen presenting cells. The monoclonal antibody acts as a "vector" or "delivery vehicle" for targeting foreign antigens onto such recipient cells. This targeting facilitates subsequent antigen recognition by helper T-cells, which are pivotal in helping the induction of antigen-specific IgG responses.

=> e cates, george a/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | CATES, DIANA M/IN |
| E2 | USPAT | 1 | CATES, DUDLEY F/IN |
| E3 | USPAT | 0 | --> CATES, GEORGE A/IN |
| E4 | USPAT | 2 | CATES, GLENN F/IN |
| E5 | USPAT | 7 | CATES, GORDON D JR/IN |
| E6 | USPAT | 1 | CATES, GORDON O/IN |
| E7 | USPAT | 1 | CATES, GUY L/IN |
| E8 | USPAT | 1 | CATES, H ALTON/IN |
| E9 | USPAT | 1 | CATES, HAROLD/IN |
| E10 | USPAT | 1 | CATES, HAROLD T/IN |
| E11 | USPAT | 2 | CATES, HENRY J JR/IN |
| E12 | USPAT | 3 | CATES, JAMES C/IN |

=> e catarini, judith e/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 3 | CATAPANO, SALVATORE J/IN |
| E2 | USPAT | 1 | CATAPANO, SHARON A/IN |
| E3 | USPAT | 0 | --> CATARINI, JUDITH E/IN |
| E4 | USPAT | 2 | CATARIOUS, JOSEPH/IN |
| E5 | USPAT | 1 | CATARIOUS, JOSEPH B/IN |
| E6 | USPAT | 1 | CATARSI, PAOLO/IN |
| E7 | USPAT | 3 | CATASTINI, ALBERTO/IN |
| E8 | USPAT | 3 | CATAUDELLA, JOHN/IN |
| E9 | USPAT | 1 | CATCH, JOHN B/IN |
| E10 | USPAT | 1 | CATCHEN, GARY L/IN |
| E11 | USPAT | 3 | CATCHER, MIKIE B/IN |
| E12 | USPAT | 1 | CATCHESIDES, PHILLIP/IN |

=> e caterini, judith e/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | CATERINACCI, JOHN/IN |
| E2 | USPAT | 3 | CATERINACCI, JOHN R/IN |
| E3 | USPAT | 0 | --> CATERINI, JUDITH E/IN |
| E4 | USPAT | 1 | CATERINI, RICHARD/IN |
| E5 | USPAT | 1 | CATERINO, GARRET J/IN |
| E6 | USPAT | 1 | CATERISANO, TERRY A/IN |
| E7 | USPAT | 1 | CATERISANO, WILLIAM P/IN |
| E8 | USPAT | 1 | CATERO, RICHARD D/IN |
| E9 | USPAT | 2 | CATERPILLAR TRACTOR CO/IN |
| E10 | USPAT | 2 | CATERSON, BRUCE/IN |
| E11 | USPAT | 1 | CATES, ALLEN A/IN |
| E12 | USPAT | 1 | CATES, ALLEN E/IN |

=> e klein, michael h/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | KLEIN, MICHAEL F/IN |
| E2 | USPAT | 1 | KLEIN, MICHAEL G/IN |
| E3 | USPAT | 0 | --> KLEIN, MICHAEL H/IN |
| E4 | USPAT | 1 | KLEIN, MICHAEL JAMES/IN |
| E5 | USPAT | 1 | KLEIN, MICHAEL L/IN |
| E6 | USPAT | 2 | KLEIN, MICHAEL N/IN |
| E7 | USPAT | 2 | KLEIN, MICHAEL T/IN |
| E8 | USPAT | 1 | KLEIN, MICHAEL V/IN |
| E9 | USPAT | 11 | KLEIN, MICHEL/IN |
| E10 | USPAT | 28 | KLEIN, MICHEL H/IN |
| E11 | USPAT | 3 | KLEIN, MICHEL HENRI/IN |
| E12 | USPAT | 1 | KLEIN, MILES/IN |

=> e klein, michel h/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | KLEIN, MICHAEL V/IN |
| E2 | USPAT | 11 | KLEIN, MICHEL/IN |
| E3 | USPAT | 28 | --> KLEIN, MICHEL H/IN |
| E4 | USPAT | 3 | KLEIN, MICHEL HENRI/IN |
| E5 | USPAT | 1 | KLEIN, MILES/IN |
| E6 | USPAT | 1 | KLEIN, MILTON/IN |
| E7 | USPAT | 6 | KLEIN, MILTON L/IN |
| E8 | USPAT | 1 | KLEIN, MIRIAM TRAVIS/IN |
| E9 | USPAT | 1 | KLEIN, MORRIS M/IN |
| E10 | USPAT | 1 | KLEIN, MORRIS R/IN |
| E11 | USPAT | 1 | KLEIN, MORTON/IN |
| E12 | USPAT | 1 | KLEIN, MYRA/IN |

=> s e2 or e3 or e4

11 "KLEIN, MICHEL"/IN
28 "KLEIN, MICHEL H"/IN

09/007,093

3 "KLEIN, MICHEL HENRI"/IN
L3 42 "KLEIN, MICHEL"/IN OR "KLEIN, MICHEL H"/IN OR "KLEIN, MICHE
L H ENRI"/IN

=> s l3 and apc

2172 APC
189 APCS
2235 APC
(APC OR APCS)
L4 7 L3 AND APC

=> d l4 1-7 leg ab

US PAT NO: 5,877,298 [IMAGE AVAILABLE] L4: 1 of 7
DATE ISSUED: Mar. 2, 1999
TITLE: Acellular pertussis vaccines and methods of preparing thereof
INVENTOR: Raafat E. F. Fahim, 524 Ceremonial Drive, Mississauga, Ontario, Canada, L5R 2T2
John R. Vose, 54 bis Route de Paris, 69260 Charbonnieres-les-Bains , Ontario, France
John Thipphawong, 45 Carlton Street Apt. 602, Toronto, Ontario, Canada, M5B 2H9
Luis Barreto, 53 Crooked Stick Crescent, Concord, Ontario, Canada, L4K 1P4
Gail E. D. Jackson, 10 Annette Gate, Richmond Hill, Ontario, Canada, L4C 5P3
Larry U. L. Tan, 2424 Folkway Drive, Mississauga, Ontario, Canada, L5L 3N3
Andrew Herbert, 199 Upper Canada Drive, North York, Ontario, Canada, M2P 1T3
**Michel H. Klein**, 16 Munro Boulevard, Willowdale, Ontario, Canada, M2P 1B9
APPL-NO: 08/433,646
DATE FILED: May 4, 1995
ART-UNIT: 187
PRIM-EXMR: Paula K. Hutzell
ASST-EXMR: Patricia A. Duffy
LEGAL-REP: Sim & McBurney

US PAT NO: 5,877,298 [IMAGE AVAILABLE] L4: 1 of 7

ABSTRACT:
A fimbrial agglutinogen preparation is prepared from a bordetella strain, particularly a B. pertussis strain, by a multiple step procedure involving extraction of the fimbrial agglutinogens from cell paste and concentrating and purifying the extracted material. The fimbrial agglutinogen preparation may be used to prepare acellular pertussis vaccines with other pertussis antigens, including pertussis toxin or toxoid thereof, the 69 kDa protein and filamentous hemagglutinin and other Bordetella antigens.

US PAT NO: 5,837,250 [IMAGE AVAILABLE] L4: 2 of 7
DATE ISSUED: Nov. 17, 1998
TITLE: Adjuvant compositions
INVENTOR: Ali Kandil, Willowdale, Canada
Olive A. James, Toronto, Canada
**Michel H. Klein**, Willowdale, Canada
Pele Chong, Richmond Hill, Canada
ASSIGNEE: Connaught Laboratories Limited, North York, Canada (foreign corp.)
APPL-NO: 08/483,856
DATE FILED: Jun. 7, 1995
ART-UNIT: 168
PRIM-EXMR: Ponnathapura Achutamurthy
ASST-EXMR: Phuong T. Bui
LEGAL-REP: Sim & McBurney

US PAT NO: 5,837,250 [IMAGE AVAILABLE] L4: 2 of 7

ABSTRACT:
Adjuvant compositions for modulating an immune response to an antigen administered to a host comprise a mineral salt adjuvant and at least one other adjuvant. The compositions provide an adjuvanting effect on an antigen which is greater than the adjuvanting effect attainable by one of the adjuvants alone. An antigen is covalently bonded to a glycolipid analog to provide a discrete molecule which exhibits an enhanced adjuvanting effect on the antigen which is greater than the adjuvanting effect attainable in the absence of such covalent bonding.

US PAT NO: 5,808,024 [IMAGE AVAILABLE] L4: 3 of 7
DATE ISSUED: Sep. 15, 1998
TITLE: Nucleic acids encoding high molecular weight major outer membrane protein of moraxella
INVENTOR: Ken Sasaki, 1131 Steeles Avenue, West, Apt. No. 512, Willowdale, Ontario, Canada, M2R 3W8
Robin E. Harkness, 640 Sheppard Avenue, East, Apt. #1706, Willowdale, Ontario, Canada, M2K 1B8
Sheena M. Loosmore, 70 Crawford Rose Drive, Aurora, Ontario, Canada, L4G 4R4
**Michel H. Klein**, 16 Munro Boulevard, Willowdale, Ontario, Canada, M2P 1B9
APPL-NO: 08/478,370
DATE FILED: Jun. 7, 1995
ART-UNIT: 182
PRIM-EXMR: Stephen Walsh
ASST-EXMR: Kenneth A. Sorensen

US PAT NO: 5,808,024 [IMAGE AVAILABLE] L4: 3 of 7

ABSTRACT:
An isolated and purified outer membrane protein of a Moraxella strain, particularly M. catarrhalis, has a molecular mass of about 200 kDa. The about 200 kDa outer membrane protein as well as nucleic acid molecules encoding the same are useful in diagnostic applications and immunogenic compositions, particularly for in vivo administration to a host to confer protection against disease caused by a bacterial pathogen that produces the about 200 kDa outer membrane protein or produces a protein capable of inducing antibodies in a host specifically reactive with the about 200 kDa outer membrane protein.

US PAT NO: 5,780,606 [IMAGE AVAILABLE] L4: 4 of 7
DATE ISSUED: Jul. 14, 1998
TITLE: Neisseria meningitidis capsular polysaccharide conjugates
INVENTOR: Ali Kandil, Willowdale, Canada
Pele Chong, Richmond Hill, Canada
**Michel H. Klein**, Willowdale, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 08/474,392
DATE FILED: Jun. 7, 1995
ART-UNIT: 163
PRIM-EXMR: Kathleen K. Fonda
LEGAL-REP: Sim & McBurney

US PAT NO: 5,780,606 [IMAGE AVAILABLE] L4: 4 of 7

ABSTRACT:
Capsular polysaccharides containing multiple sialic acid residues, particularly the Group B polysaccharide of Neisseria meningitidis, are modified by chemical reaction to randomly introduce pendant reactive residues of heterobifunctional linker molecules to the polysaccharide backbone. The capsular polysaccharide is deacetylated and the heterobifunctional linker molecule is reacted with the deacetylated material and any residual amino groups are blocked by reaction with alkyl acid anhydride. The introduction of the linker molecules to the polysaccharide chain between the termini enables the polysaccharide to be linked to a carrier molecule, such as a protein, to enhance the immunogenicity of the polysaccharide. The conjugate molecule may be formulated as an immunogenic composition for raising antibodies in a host to the polysaccharide.

US PAT NO: 5,708,149 [IMAGE AVAILABLE] L4: 5 of 7
DATE ISSUED: Jan. 13, 1998
TITLE: Method for producing purified recombinant Haemophilus influenzae transferrin binding proteins
INVENTOR: Sheena Loosmore, Aurora, Canada
Robin Harkness, Willowdale, Canada
Anthony Schryvers, Calgary, Canada
Pele Chong, Richmond Hill, Canada
Scott Gray-Owen, Calgary, Canada
Yan-Ping Yang, Willowdale, Canada
Andrew Murdin, Newmarket, Canada
**Michel Klein**, Willowdale, Canada
ASSIGNEE: Connaught Laboratories Limited, North York, Canada (foreign corp.)
APPL-NO: 08/487,890
DATE FILED: Jun. 7, 1995
ART-UNIT: 185
PRIM-EXMR: Nancy Degen
ASST-EXMR: Matthew Latimer
LEGAL-REP: Sim & McBurney

US PAT NO: 5,708,149 [IMAGE AVAILABLE] L4: 5 of 7

ABSTRACT:
Purified and isolated nucleic acid is provided which encodes a transferrin receptor protein of a strain of Haemophilus or a fragment or an analog of the transferrin receptor protein. The nucleic acid sequence may be used to produce peptides free of contaminants derived from bacteria normally containing the Tbp1 or Tbp2 proteins for purposes of diagnostics and medical treatment. Furthermore, the nucleic acid molecule may be used in the diagnosis of infection. Also provided are recombinant Tbp1 or Tbp2 and methods for purification of the same. Live vectors expressing epitopes of transferrin receptor protein for vaccination are provided.

US PAT NO: 5,681,570 [IMAGE AVAILABLE] L4: 6 of 7
DATE ISSUED: Oct. 28, 1997
TITLE: Immunogenic conjugate molecules
INVENTOR: Yan-ping Yang, Willowdale, Canada
Ali Kandil, Willowdale, Canada
Lucy Gisonni, Toronto, Canada
Raafat Emil Fahmy Fahim, Mississauga, Canada
**Michel Henri Klein**, Willowdale, Canada
ASSIGNEE: Connaught Laboratories Limited, North York, Canada (foreign corp.)
APPL-NO: 08/371,965
DATE FILED: Jan. 12, 1995
ART-UNIT: 182
PRIM-EXMR: James C. Housel
ASST-EXMR: Jennifer Shaver

US PAT NO: 5,681,570 [IMAGE AVAILABLE] L4: 6 of 7

ABSTRACT:
Immunogenic conjugate molecules comprising at least a portion of a capsular polysaccharide of a Streptococcus strain linked to at least a portion of an outer membrane protein of a Haemophilus strain are provided in which the immunogenicity of the capsular polysaccharide is increased. Particularly capsular polysaccharide from Streptococcus pneumoniae are linked to an outer membrane protein of a Haemophilus influenzae strain, which protein may be the P1, P2 or particularly the P6 outer membrane protein. Conjugate molecules comprising the P6 protein linked to a capsular polysaccharide from an encapsulated pathogen other than Streptococcus also are described, in which the immunogenicity of the capsular polysaccharide is enhanced. Such conjugate molecules may be incorporated into immunogenic compositions for protecting a host against disease caused by the Streptococcus strain and preferably also the Haemophilus strain. The conjugate molecules and antibodies specific for the capsular polysaccharide or specific for the outer membrane protein may be employed in diagnostic procedures and kits. A process for individually isolating P1, P2 and P6 outer membrane proteins from a Haemophilus strain also is provided.

09/007,093

US PAT NO: 5,679,352 [IMAGE AVAILABLE] L4: 7 of 7
DATE ISSUED: Oct. 21, 1997
TITLE: Synthetic Haemophilus influenzae conjugate vaccine
INVENTOR: Pele Chong, Richmond Hill, Canada
Ali Kandil, Willowdale, Canada
Charles Sia, Thornhill, Canada
Michel Klein, Willowdale, Canada
ASSIGNEE: Connaught Laboratories Limited, Willowdale, Canada (foreign corp.)
APPL-NO: 08/475,989
DATE FILED: Jun. 7, 1995
ART-UNIT: 185
PRIM-EXMR: Mindy Fleisher
ASST-EXMR: Nancy J. Degen
LEGAL-REP: Sim & McBurney

US PAT NO: 5,679,352 [IMAGE AVAILABLE] L4: 7 of 7

ABSTRACT:
Synthetic peptides have an amino acid sequence corresponding to at least one antigenic determinant of at least one protein, usually a structural protein, particularly the P1, P2 and P6 protein, of Haemophilus influenzae (Hi), particularly type b, and are used as is, in chimeric T-B form, in lipidated form, linked to a carrier molecule, particularly a synthetic PRP molecule and/or polymerized to form molecular aggregates, in vaccines against Hi.

=> d his

(FILE 'USPAT' ENTERED AT 16:18:18 ON 30 MAR 1999)
L1 6 S (ANTIBOD? OR MONOCLON?)(P)(CONJUGATE OR FUSION PROTEIN O
R C
E ANAND, NAVEEN/IN
E BARBER, BRIAN H/IN
L2 3 S E3
E CATES, GEORGE A/IN
E CATARINI, JUDITH E/IN
E CATERINI, JUDITH E/IN
E KLEIN, MICHAEL H/IN
E KLEIN, MICHEL H/IN
L3 42 S E2 OR E3 OR E4
L4 7 S L3 AND APC

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
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U.S. Patent & Trademark Office LOGOFF AT 16:27:29 ON 30 MAR 1999